DRUG & COSMETIC INDUSTRY

SEPTEMBER 1959

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Important Riboflavin Development

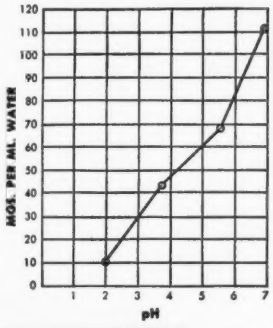
✓ Higher solubility ✓ Better taste

✓ No solubilizer needed ✓ Commercial production

USE ROCHE RIBOFLAVIN 5′-PHOSPHATE SODIUM

higher solubility

Now you can make clear solutions with a concentration of 30 mg. or higher per ml. of water when you use the new Roche riboflavin-5′-phosphate sodium. No longer do you need to use solubilizers and special techniques to achieve a satisfactory solution. Remember the trouble you had in getting a solution of even 2 mg. of riboflavin per ml.? Those days are now past.



SOLUBILITY of Roche riboflavin-5′-phosphate sodium in water at different pH levels; room temperature.

These data show that solubility of Roche B_2 phosphate sodium depends on hydrogen ion concentration in water. It is useful to note that the solubility of riboflavin U.S.P. (approximately 0.12 mg. per ml.) inserted on graph would fall just above the base line.

specifications

Tests show that B_2-5′ (M.W. 514.4) has the full theoretical activity on the molecular basis of riboflavin (M.W. 376.36). Theoretically one gram of the phosphate is equivalent to 0.73 grams of riboflavin. The Roche product contains small amounts of moisture, disodium salt, diphosphate ester and unesterified riboflavin. It has a riboflavin activity of 70-73% by weight.

biological availability

Roche riboflavin-5′-phosphate sodium has immediate biological activity because it is identical with the natural flavin mononucleotide occurring in the "yellow" respiratory tissue enzyme system.

better taste

Roche riboflavin-5′-phosphate sodium does not have the intensely bitter taste of riboflavin itself. It is more palatable in high concentrations. The different taste is of definite advantage in oral preparations.

solubility—taste demonstration

You can prove to yourself, easily and quickly, the solubility-taste advantages of Roche riboflavin-5′-phosphate sodium with the Roche demonstration kit. Ask your Roche representative to show it to you. Or we'll be glad to send one, without charge, at your request.

cost comparison

Even though the cost of Roche B_2-5′ is somewhat higher than regular riboflavin, its use can result in actual savings. You eliminate expensive solubilizers and unnecessarily large amounts of niacinamide. You reduce or eliminate costly complaints and returns. You are able to make manufacturing economies.

stability

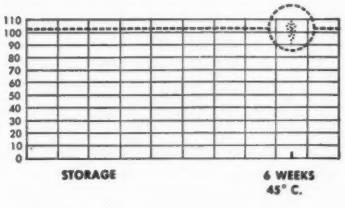


Chart demonstrates stability of Roche product in B-complex parenteral solutions with and without vitamin C over wide potency range.

uses

The new riboflavin-5′-phosphate sodium, probably the most important riboflavin development since Roche introduced the vitamin commercially in 1941, is specially designed for use in manufacturing:

- **pharmaceutical** vitamin injectable solutions, drops and elixirs, gelatin capsules and chewable tablets
- **food enrichment,** especially if by liquid application

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Drug and Cosmetic Industry

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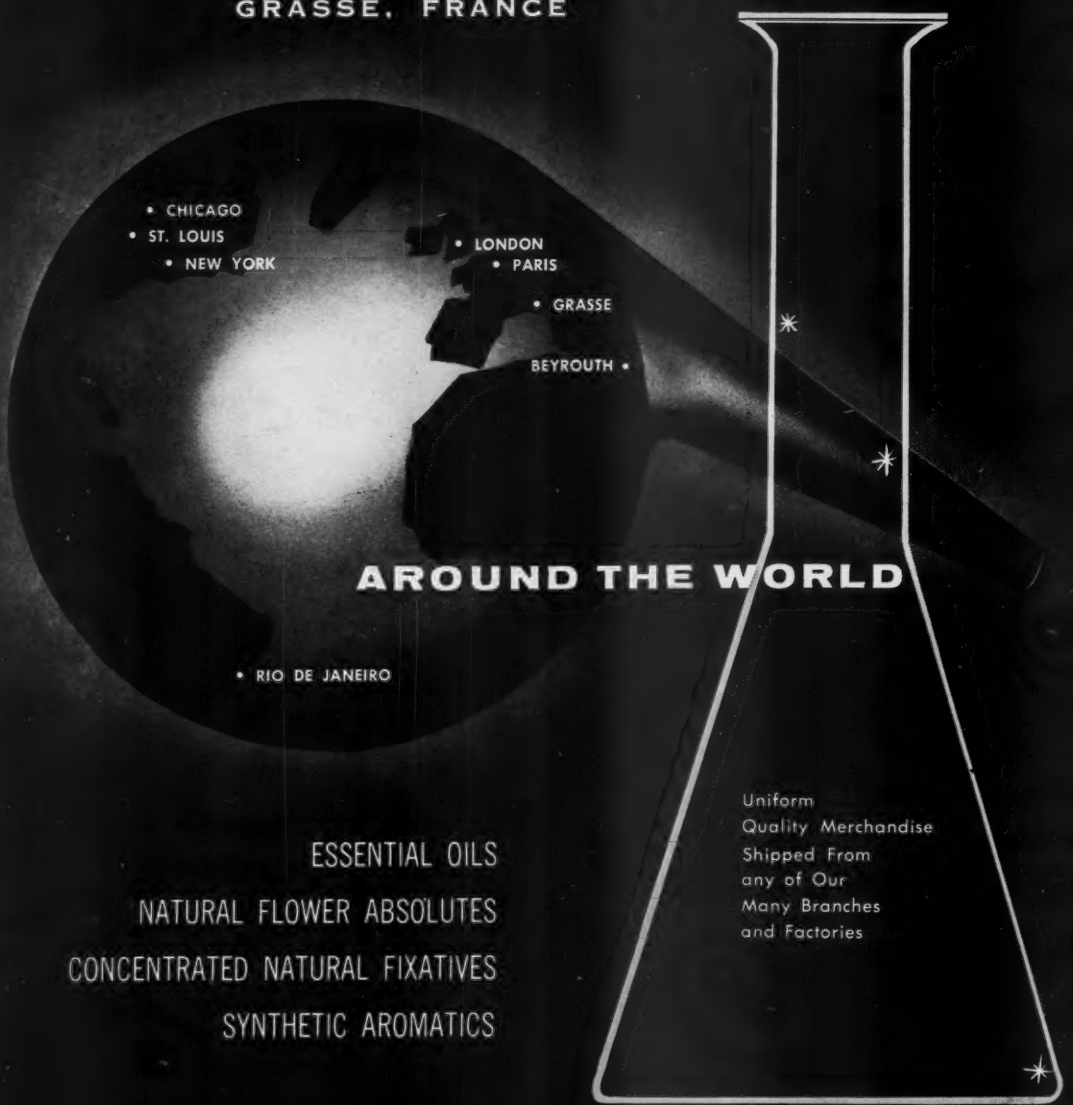

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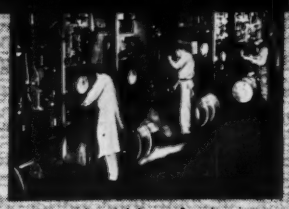

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You may wish to check certain items in this advertisement and forward to those concerned in your company.

ROUTE TO:

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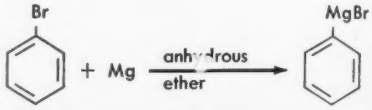
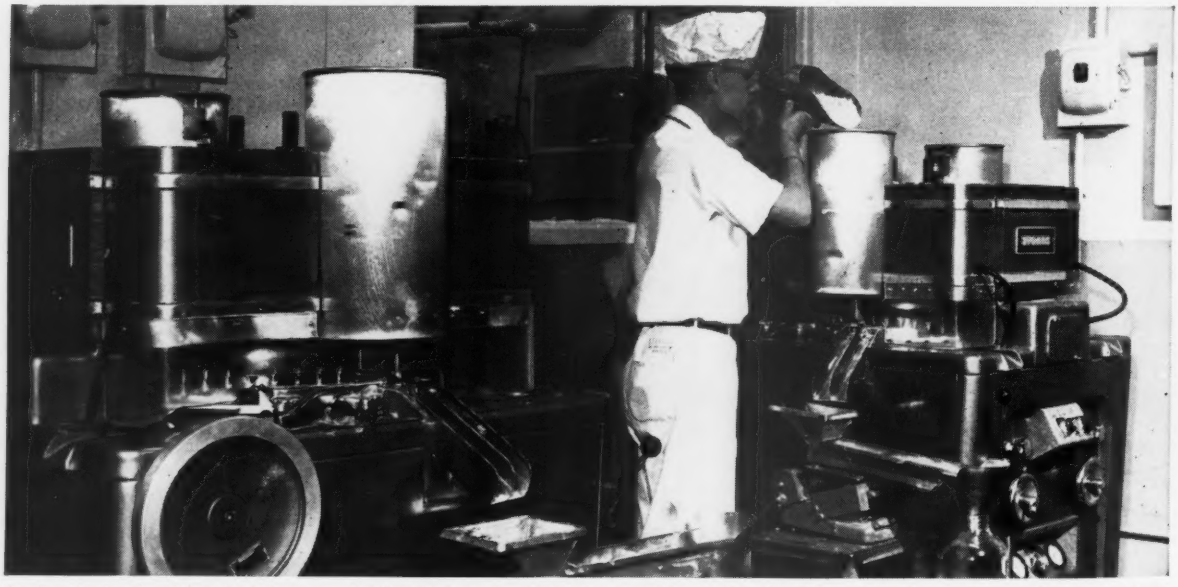


Bromobenzene is likewise a valuable intermediate in the Friedel-Crafts reaction, and it and its derivatives may also be sulfonated or nitrated. From the production standpoint, bromobenzene is a remarkably stable compound



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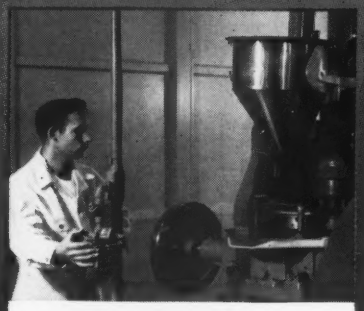

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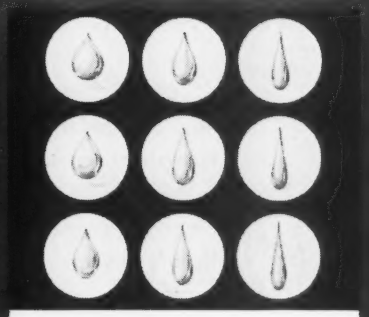

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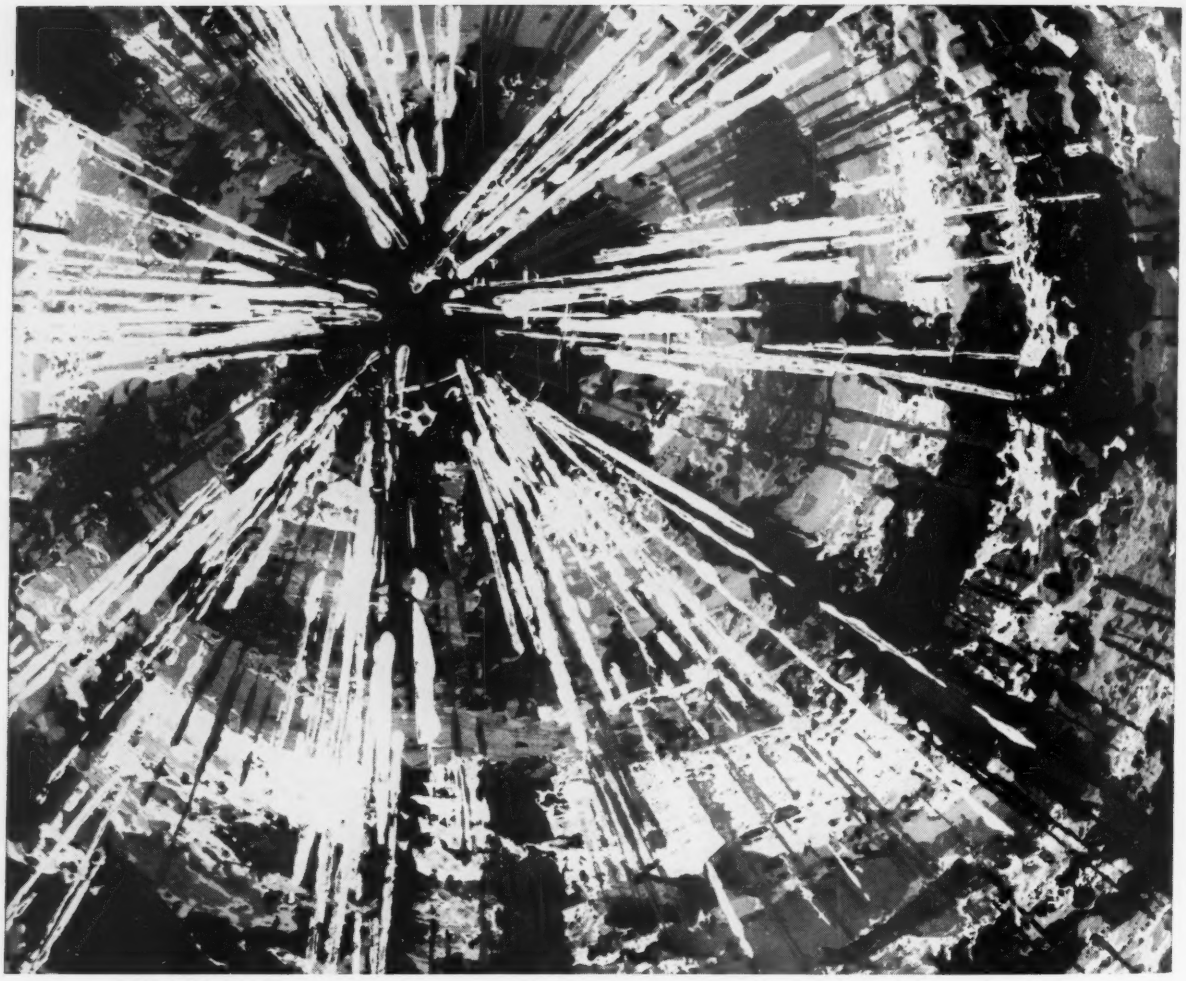

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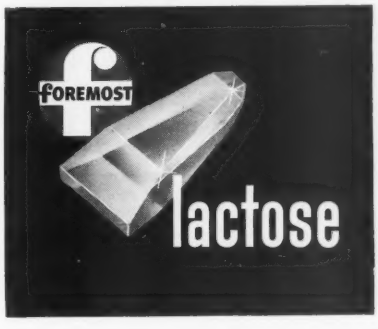

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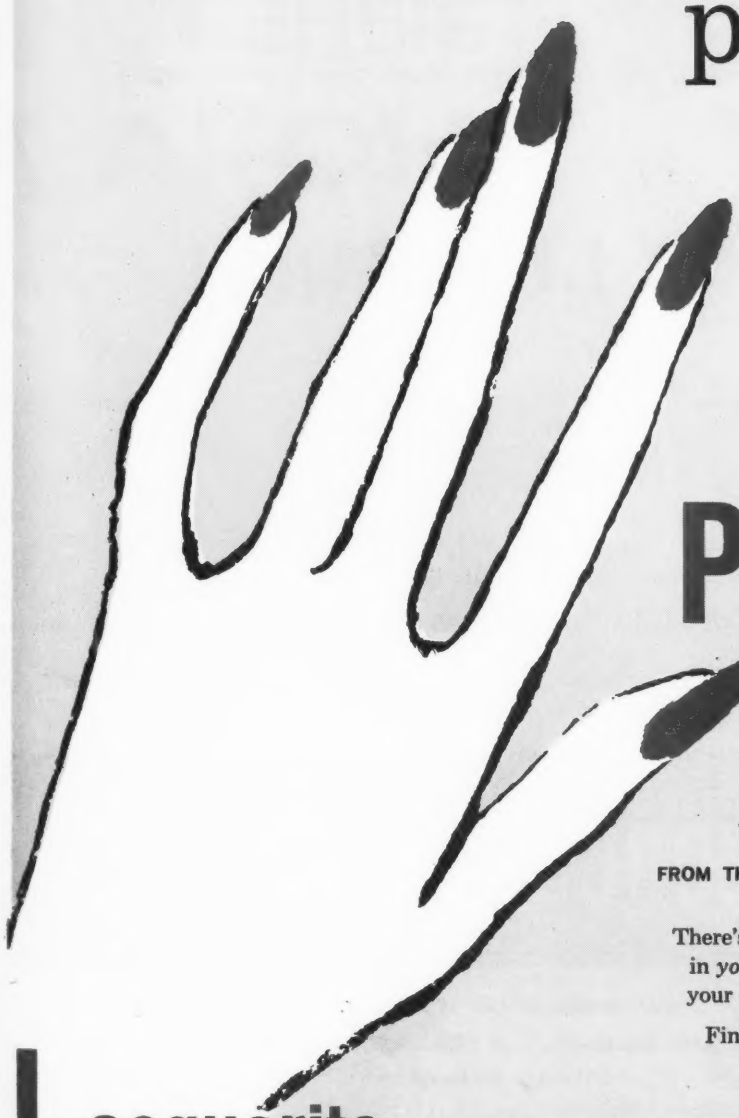

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Detergents at New High

Soap and synthetic detergent sales for the first six months of 1959 established a new high in tonnage of 2,062,686,000 pounds, up 4.9 per cent from the first half of 1958, and a new high in sales value of $526,142,000, up 6.2 per cent. Synthetic detergents sales totaled 1,540,602,000 pounds valued at $372,996,000, an increase of 7.9 per cent in tonnage, and 6.9 per cent in dollars. Sales of liquid synthetic detergents continue to expand with particular strength in packaged liquids. Total liquid detergent sales were 267,480,000 pounds valued at $97,467,000, up 32.2 per cent in pounds and 29.4 per cent in dollars compared with the first six months of 1958. Solid synthetic detergent sales totaled 1,273,122,000 pounds valued at $275,529,000, a 3.9 per cent incease in quantity, and a 0.7 per cent increase in dollars.

Soap sales amounted to 522,084,000 pounds valued at $153,146,000, off 3 per cent in poundage, but up 4.4 per cent in value.

Wiliam H. Rorer, Inc. Facts

William H. Rorer, Inc., capital stock was offered last month, the amount being 90,000 shares at $48.75 per share. The stock was being sold in equal amounts of 45,000 shares each by Herbert C. Rorer, chairman of the board, and Gerald F. Rorer, president, each of whom will receive a net amount of slightly over $2 million for the shares they have sold. Outstanding stock of the company totals 837,837 shares of 33 1/3 cents per share. After selling the 90,000 shares, Herbert C. Rorer owns 21 per cent, and Gerald F. Rorer owns 22.6 per cent of the outstanding shares, and 412,599 shares, or approximately 49.2 per cent of the outstanding stock is owned by members of the Rorer family.

The company makes ethical drug products, the main one of which is Maalox, used for gastric hyperacidity, peptic ulcers, and gastritis. It accounted for about 80 per cent of 1958 net sales, which totaled $6,617,156. Mainly because of the introduction of Maalox in 1949 and an expanded sales program started the same year, the annual sales have risen from about $850,00 in 1950 to $1,847,000 in 1954, and to more than $6.6 million in 1958. Earnings have increased from about $30,000 in 1950, to about $150,000 in 1954, and to $830,000 in 1958. Sales for the first six months of 1959 were $3,707,710, against sales for the first six months of 1958 of $2,578,862. Profits for these periods were $424,068, and $212,679.

Since 1949 the company has established a training program for detail men, which now number 215. The company has about 400 employes of which 110 are production workers. The company has a salesmen's fleet of automobiles valued at $430,875.

The company owns a plant in Philadelphia subject to mortgage of $128,362. Plans call for a new and larger plant and research facilities in the Philadelphia area within the next few years at a cost of approximately $1.5 million.

Besides Maalox, the more important specialty products of the company are Ascriptin, a pain reliever; Chardonna, for sedation; Fermatin, for anemia; Fermalox, for iron deficiency anemia; Parepectolin, for diarrhea. Other products of lesser importance are: Comfortine, baby ointment; Probutylin, for nausea; Tablet Lumaspirin with Hyoscyamus, pain reliever and sedative; Neoxyn, for poison ivy; Nurokardiac, for nervous heart; Tertiasul, a sulfonamide; and Carfusin, for athlete's foot.

Firmenich Plant

Firmenich, world famous Swiss firm, a leader in the field of serious research and production of synthetic organic chemicals for perfumery and flavor purposes, has purchased the Ciba manufacturing plant and facilities located on a 113-acre site at Kimberton, Pa. The plant, comprising 65,000 square feet, was constructed and modernized in 1954. Firmenich has not formally announced future plans, but it can

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be presumed they will initiate production of their aromatic chemical specialties in the United States.

Revlon Enters Hair Coloring

Revlon has entered the hair coloring field through the acquisition of Bressard Hair Products Corporation and Bressard Distributors, Inc. These companies make and distribute Bressard Tiara hair coloring and hair conditioning products, which are sold, through beauty distributors, to beauty salons for professional use. The company's main manufacturing plant is in New York and it conducts training schools for Bressard Tiara operators in New York, Chicago, Los Angeles, Miami, Boston, and Atlanta. The company was established in June, 1951.

FDA and NIH Budgets Up

The Food and Drug Administration will have $2,283,000 for its operations during the next fiscal year in accordance with the appropriation bill for the Department of Health, Education, and Welfare, signed by President Eisenhower. The appropriation for the next year is $13.8 million, an increase of 26 per cent.

HEW received $3.45 billion for fiscal 1960, compared with $3.24 billion for the current year. Of this amount $400 million, a 36 per cent increase from the current year, and a four-fold boost in the last six years, will be for the National Institutes of Health as follows: General Research $45,994,000; Cancer, $91,257,000; Mental Health, $68,090,000; Heart, $62,237,000; Dental Health, $10,019,000; Arthritis, $46,862,000; Allergy, $34,054,000; Neurology, $41,487,000.

President Eisenhower expressed misgivings about the NIH increase for the following reasons:

The steep rise might lower the quality of research projects supported by an increasing flow of grant applications more rapidly than the procedure for their careful appraisal can be effectively applied. It might cause too great a diversion into research of the manpower and other resources needed for equally vital teaching and medical practice. It might result in the substitution of federal funds for non-federal support of medical research and training, and discourage further expansion of such support.

President Eisenhower said that these effects "can work against the very goal being sought—improved health for all American people." Therefore, he is asking HEW Secretary and the Surgeon General of the Public Health Service to keep in mind three things when they consider any new research or training program:

(1) That it is of such high priority and great promise that its deferment would be likely to defer progress in medical discovery.

(2) That it will not result in the harmful diversion of manpower and other resources needed for teaching and medical care service.

(3) That it will not bring about the substitution of federal for non-federal sources of support for medical research and training.

U. S. Savings Stamps as Premiums

The "Own a Bit of America Savings Bond and Stamp" program was officially launched on the steps of the Sub-Treasury Building in New York in September, on the 170th anniversary of the founding of the United States Treasury Department.

Marshall S. Lachner, president of B. T. Babbitt, Inc., presented details of OBA Corporation program in which his company is participating. "We see this OBA plan as an important device to help increase the sales of U. S. Government Savings Stamps and Bonds," he said. "This program costs the government nothing. Manufacturers participating pay all the costs for advertising the plan through which customers get free Treasury Stamps with products manufactured by companies participating in the plan. And, it costs the consumer nothing, for the price of the product remains the same."

Vita-Yums, and Charles Antell's Hair Spray, Formula 9, Liquid Shampoo, and Creme Shampoo, are on the list as well as the many cleansing products which are produced by Babbitt. It will be recalled that some while back Babbitt inaugurated the scheme of giving away with each package of their products a coupon, three of which would buy a fifteen-cent subway token.

Fischelis Retires from A.Ph.A.

Dr. Robert P. Fischelis retired as secretary and general manager of the American Pharmaceutical Association at the annual meeting of the association held last month, and has been succeeded by Dr. William S. Apple, who was named secretary-nominate in April 1958 and since that time has been serving as assistant secretary of the association.

Having reached retirement age, Dr. Fischelis retired from a post he had held with distinction since 1945. For over fifty years he has been active in retail, hospital, and manufacturing pharmacy; education; research and survey work; journalism; and association activities. In 1943 he was awarded the Remington medal; in 1952, the Lascoff Award and the Ernst T. Urban Medal of the Pharmaceutical Society of Germany. He was also honored by the pharmaceutical associations of Cuba and Argentina; in 1956 he received the Alumni Award of the Philadelphia College of Pharmacy and Sciences; and in 1957 he received the American Druggist Man of the Year Award for 1956.

At present Dr. Fischelis is president of the National Drug Trade Council, president of Friends of Historical Pharmacy, consultant to the Surgeon General of the U. S. Army, consultant on the government Medicare program; honorary consultant to the Surgeon General of the U. S. Navy, and to the Surgeon

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General of the Public Health Service on the National Health Survey.

Dr. Fischelis will continue to live in Washington where he will carry on consultant activities in pharmacy, pharmaceutical education and research.

At the closing banquet of the 1959 convention of the A.Ph.A., Dr. Fischelis was presented with a beautiful volume bound in rich red morocco containing 15 years of his monthly "Straight from Headquarters" reports. It includes his monthly articles, starting in February 1945, when he assumed office, and continuing through August 1959.

Vitamin Foundation Figures

The National Vitamin Foundation, supported solely by 24 producers and distributors of vitamins and related products, has appropriated since its inception in 1946 through 1958 a total of $1,456,622.70 for the support of nutrition research. In addition, the Foundation appropriated over these years $266,449.28 for educational purposes, making total expenditures of $1,723,071.98 by this non-profit, industry-supported scientific organization.

Appropriations for research grants were divided as follows: Vitamin A, $132,836.50; Vitamin D, $9,200; Vitamin E, $109,350; or a total for fat soluble vitamins of $251,386.50. For B Vitamins, a total of $1,073,435.70, divided as follows: B_{12}, $287,396.62; Folic Acid, $117,262.50; Biotin, $21,425; B_6, $210,635.86; Pantothenic Acid, $145,094.59; Riboflavin, $43,755; Other B Vitamins and Miscellaneous, $247,866.13. The remaining $131,800.50 was spent for research in Vitamin C, $59,764; Flavonoids, $20,100; Amino Acids, Proteins, and Fats, $51,936.50.

Of the total for research grants, $709,825.98 was spent for studies of man; $542,042.39 for studies of the experimental animal; $131,954.33 for microbiology, enzymology, and chemistry; and $72,800 for studies of farm animals.

PMA Moves in Washington

The Pharmaceutical Manufacturers Association has moved its headquarters in Washington to 1411 K Street, N.W., Washington 5, D.C. The New York office of the association on Rockefeller Plaza has been closed and Dr. J. O'Neill Closs, Administrative Vice-President, is now located at the Washington office. The headquarters of the association now occupy the thirteenth floor of a new building. Telephone number is unchanged (NAtional 8-6435).

Governor Meyner Lauds Tranquilizers

Governor Robert B. Meyner of New Jersey said that the development of tranquilizing drugs is "one of the greatest services of the drug industry."

Addressing the Pharmacy Education-Industry Forum of the National Pharmaceutical Council, he said mental illness, "a subject close to my heart and mind . . . is one of the most distressing human problems with which a governor must deal." Four years ago he personally urged increased legislative appropriations for tranquilizing drugs, he said. Since statewide use of these drugs, mental patients have responded to therapy, "become less restrained," and hospitals have been able to "grant more freedom to patients, and hence speed their return to normal lives."

Olin-Mathieson Expansion

In a $30 million expansion program, Olin Mathieson Chemical Corporation plans construction of new facilities for production of glycerin, epichlorhydrin, propylene oxide, propylene glycol, and polypropylene glycols at Brandenburg, Ky.; doubling of production of Poly-Solv ethers, Poly-Tergent surfactants and ethylene at Brandenburg; production of sulfamic acid at Joliet, Ill.; and improvement of chlorine facilities at Niagara Falls, N. Y.

"Black and White Magic"

A Post Office hearing examiner has ruled that advertising of a book called "Black and White Magic" is a fraudulent scheme for obtaining money through the mails. Among other things, the book tells how to get the best gambling hand, as follows:

"You will take the nutmeg of India, in which you will drill a hole in which you will pour the pure mercury and seal it with pure wax. After this take a chamois bag, in this bag you will put a piece of highly magnetic green lode stone, lucky hand, silver magnetic sand, John the Conquerer root, devil shoe string, and the five finger grass, then on top of this you will place the prepared nutmeg of India. This done, seal the bag by sewing it all the way around so that none of articles may fall out, and on the outside sprinkle three drops of Jockey Club perfume, one every week."

The company selling the book also sells the exotic objects named.

Fair Trade in the States

There are 31 states of the Union that have effective fair trade laws, plus Ohio, which state has a new law becoming effective October 22 to replace one that was invalidated by the courts. Of the 31 states there are 18 with laws that have been found valid by the high courts of these states and by the U. S. Supreme Court. These states are: Arizona, California, Connecticut, Delaware, Hawaii, Illinois, Maryland, Massachusetts, Mississippi, New Jersey, New York, North Carolina, Pennsylvania, Rhode Island, South Dakota, Tennessee, Washington, Wisconsin.

The other 13 states which have effective fair trade laws, but on which there has ben no adjudication by the high courts, are: Alabama, Idaho, Iowa, Kansas, Maine, Minnesota, Montana, Nevada, New Hampshire, North Dakota, Oklahoma, Virginia, Wyoming. There are four states in which there never have been fair trade laws (as well as the District of Columbia).

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Gattefosse SFPA, for Institute Merieux, Lyon, France.

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There are 12 states in which the fair trade laws have been invalidated as far as the non-singer clause is concerned. These are: Arkansas, Colorado, Florida, Georgia, Indiana, Kentucky, Louisiana, Michigan, New Mexico, Oregon, South Carolina, West Virginia. And there are two states in which the entire fair trade laws were entirely invalidated by the courts. These are Nebraska and Utah.

Russia and the Health Front

Russia has mounted a medical offensive directed principally at developing areas, according to John T. Connor, president of Merck & Co., and is "moving into inviting vacuums on the health front." He urged "mobilization of America's medical resources to meet this new and infinitely more complex phase of the cold war." Mr. Connor made these statements during testimony last month in support of the International Health and Medical Research Act of 1959 before the Subcommittee on Health and Safety of the House Interstate and Foreign Commerce Committee. The measure passed the Senate by a 63-17 vote.

The proposed program of international medical research will help protect U. S. health against new and strange diseases from other parts of the world, said Mr. Connor, and will "open up new avenues for research discoveries under conditions not possible in the United States alone." Among Russian moves to fill the "inviting vacuums on the health front," Mr. Connor cited these examples: Russia's effort to take credit for proposing an International Health Year, a U. S. proposal; propaganda use of live-virus polio vaccine first developed in the United States; health teams in North Africa and South Asia; and Russia's rising production of doctors for export, trained in the languages and cultures of Asia, Africa, the Middle East, and Latin America.

Mr. Connor suggested caution in any cooperation with Russia beyond basic research and exchange projects. "Certainly," he said, "we must not lightly trade away the important technical resources of our pharmaceutical and chemical industries. If we should bargain away our hard-won American research knowledge, technical skills and production know-how, we will be handing over to Russia a valuable national asset. We would permit the Russians to free thousands of skilled scientists, engineers and technicians for military development and economic warfare, instead of taking the sensible course of requiring them to expend their own time, effort and resources in developing pharmaceutical and chemical know-how, as we have had to do."

Mr. Connor urged special attention to research in the newly developing areas of the world. He proposed provision in the bill for country-by-country health research teams, research into the "science of public health" in areas where preventive medicine is a fundamental and urgent need, and expanded training of nationals of the cooperating countries as medical personnel which would form a "permanent cadre" of medical workers in their countries.

Mr. Connor termed administration of the international research program by the National Institutes of Health "of critical importance." NIH is the only agency with the scientific and administrative skills and experience for carrying out the program, he said, adding: "Medical research should be left in the hands of medical scientists."

SK&F Wins Injunction

Smith, Kline & French Laboratories has won a preliminary injunction in the U. S. District Court in Houston, Texas, against the Crown Drug Company of Houston for unfair competition and trademark infringement. Judge Allen B. Hannay ordered Crown Drug to refrain from advertising and offering for sale imitations of any of the 12 SK&F products involved in the suit. He also prohibited the company from making any reference in its literature to any of the trademarks owned by SK&F. The Judge said that "the obvious purpose and effect" of Crown Drug's advertising was to "invite druggists to substitute and palm off" its imitation products in filling prescriptions calling for SK&F's trademarked products. The Judge said that "substitution by retail druggists of one drug for another called for by a physician's prescription is an unwarranted interference with the physician-patient relationship and a danger to public health." It is unethical, and in most states, including Texas, is condemned by law, he said. SK&F filed a complaint against Crown Drug claiming actual damages of $200,000 and requesting punitive damages of $100,000. It requested that the damages be tripled.

Flint, Eaton Bought by Baxter

Flint, Eaton, & Co., Decatur, Ill., manufacturer of pharmaceutical specialties, founded in 1897, has been acquired by Baxter Laboratories. The purchase is to be effected by an exchange of stock, the amount not being disclosed. The company will be operated as a division of Baxter Laboratories, according to Baxter president William B. Graham. C. R. Flint, board chairman of Flint, Eaton, will serve as chairman of the division, and J. K. Flint, president of Flint, Eaton, will serve as president of the division. Baxter, through its other divisions a manufacturer of pharmaceutical specialties, intravenous solutions, and enzymes, is gaining a new group of specialty prescription pharmaceuticals from Flint, Eaton. Flint, Eaton is best known for its line of lipotropic and hematinic products that account for a large share of its sales volume.

"We anticipate that the expanded sales force we will have with the acquisition of Flint, Eaton will enable us to increase our marketing programs to the nation's doctors for the new products being developed through our research," said Mr. Graham.

Baxter also gains a modern three-story pharmaceutical plant containing some 30,000 square feet of floor space at 300 E. Main Street, Decatur.

Flint, Eaton was founded by James G. Flint, grandfather of the president chairman and president. Mr. Flint died in 1927, when his son George R. Flint served as president until his death in 1954. George R. Flint was president of the American Pharmaceutical Manufacturers Association in 1935-36. Upon his death his sons assumed their roles in the management of the firm.

The company's first products were medical formulations developed by the founder. Its first venture into the prescription market was in 1925 when Ceanothyn, a hemostatic—still widely used—was introduced. in 1947, a series of lipotropic products using choline as a base were introduced after intensive research. These products, designed to counteract fatty infiltration of, and to remove fat deposits from the liver, proved to be an important contribution to medicine. The company also produced a series of Ferrolip products manufactured from iron choline citrate, a new chemical compound developed by the company. These products are for combatting deficiency anemia.

Lilly Digest Facts

Interesting facts from the Lilly Digest of Drug Store Operations for 1958 are that operating expenses have risen steadily since World War II, as in most enterprises, but in pharmacy some relief has been provided by concurrent but modest increases in gross margin. This, combined with good management of operating costs and slight increases in the proprietor's salary, has enabled pharmacy owners and managers to hold the line on total income with a measure of success.

A study of the data shows that despite the buying power of large-volume pharmacies, gross margin as a percentage of total sales is comparable to that of other sales-volume groups and is identical with that of the smallest size classification. Total income and investment in merchandise stock inventory, however, is quite another story. The percentage of sales retained as profit and salary by store owners ranges downward from 17.9 per cent in low-volume stores to 9.8 per cent in the giants of retail pharmacy. Inventory also ranges downward from 24.7 to 14.5 per cent of sales.

The owner of a retail pharmacy who devotes full time to an on-the-scene management of his business withdraws remuneration for services rendered. Normally, this withdrawl is comparable to what he would be required to pay a manager. In addition, as compensation for the risks and responsibilities assumed in store ownership, he expects to obtain a somewhat greater return from his investment than he could earn from capital invested in stocks and bonds.

As a business grows in size, the work load also grows, and the owner finds that he must rely on others to get the job done. Therefore, he is obliged to devote a greater proportion of sales to employees' wages. This expense averaged 14.9 per cent of sales among top-volume Lilly Digest pharmacies as compared with 5.2 per cent in the low-volume group. In pharmacies of the latter type, the owner himself is usually able to handle the multitude of responsibilities and thus is able to hold the line on employees' wages.

Average investment in merchandise stock inventory was 7.6 times more in large-volume pharmacies than in small-volume stores, but total sales were 13 times greater. Annual rate of turnover of merchandise stock averaged 4.4 times in the former group and 2.6 times in the latter.

Two-thirds of the nation's retail pharmacies are located east of the Mississippi River and one-third are to the west. Thirty-five per cent are in communities of less than 5,000 population and 22 per cent in metropolitan centers. About 37 per cent have annual sales of less than $50,000; 10 per cent have sales of more than $200,000 per year. Differences in operating ratios exist because of geographical locations. Substantial variation is apparent in sales volume, the range being from $107,786 in the West North Central section to $141,013 in the Pacific States—a difference of 30 per cent. During each of the five years in which geographical summaries have been published in the Digest, the Far West section has led the nation in average sales.

The growth of the prescription business is indicated by the fact that in the last ten years (1949-1958) prescription income has increased 173.2 per cent; other sales have increased 34 per cent; total sales have increased 60.5 per cent; number of prescriptions has increased 47.9 per cent; average prescription price has increased 85.0 per cent; average prescription stock inventory has increased 102.3 per cent; average nonprescription stock inventory has increased 28.6 per cent; and average total merchandise stock inventory has increased 45.9 per cent.

Musk Imports Allowed

Musk, that most valuable perfume ingredient imports of which have not been allowed since about late 1951, can now be imported directly from India. The Foreign Assets Control of the Treasury Department announced last month that "certificates of origin issued by the Ministry of Commerce and Industry of the Government of India under procedures agreed upon between that Government and the Foreign Assets Control are now available with respect to the importation (of musk) into the United States directly, or on a through bill of lading from India."

LICENSING AND IMPORTING PERFUMES UNDER TRADEMARKS*

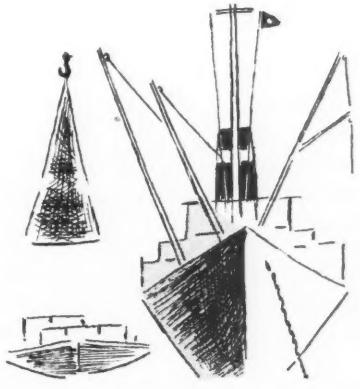
BY H. GREGORY THOMAS PRESIDENT, CHANEL, INC.

Five years ago, the Department of Justice brought civil antitrust actions against Guerlain, Corday, and Lanvin to stop them from preventing importations of their finished products from abroad, especially by American tourists. After winning in the District Court, the Government asked the Supreme Court—to which the defendants had appealed—to return the cases to the District Court so that the Government could ask for dismissal. This was effected late last year. Now the Government has introduced a bill before Congress that would remove all protection from importers of perfumes and similar products, even though these products are, according to the Federal Trade Commission, "made in the United States." It is to the subject of this bill that Mr. Thomas addresses himself.

We are faced with a legislative proposal so serious in nature that, if enacted, it would, in my opinion, have a completely disruptive effect, not only on United States importers in many industries, but also on American labor and the whole complex of our international trade relations.

Before outlining the unprecedented sweep of H.R. 7234, introduced upon the Government's request by Congressman Celler on May 19, 1959, let me set the record straight with regard to existing economic conditions in the perfume and cosmetic industry. I suggest that the instituting of the recent antitrust proceedings charging the importers with violation of the monopoly section of the Sherman Act, Section 2, as a result of the exercise of their present privilege to record their United States-owned trademark registrations with the Bureau of Customs, reflected a regrettable disregard of the highly competitive economic structure of the industry. Too, these cases show a basic misconception of the commercial and legal bases for the types of protection which independent United States distributors and importers of foreign-made merchandise enjoy today under Section 42 of the Trademark Act and Section 526 of the Tariff Act. The Celler bill would repeal the Tariff Act protection altogether and would radically change existing protection, even with regard to importation of "copies and simulations."

The Celler bill would no longer make available the infringement remedies of the Trademark Act to an American trademark owner, who has validly



acquired the United States trademark rights from a foreign manufacturer as the result of a territorial assignment or a long-term exclusive distribution agreement, and who seeks to prevent importation into or sale in the United States of a genuine foreign-made product which—to borrow a phrase from the Government's statement accompanying the introduction of the Celler bill—"legitimately" bears a registered trademark.

The Celler bill makes no distinction whatsoever between a mere distributor or agent, on the one hand, and an "independent" United States distributor or assignee, on the other. It would, therefore, go very much further than did even the District Court's decision in the perfume cases [*United States* v. *Guerlain, Inc.*, et al., 155 F. Supp. 77 (S.D.N.Y.) judgment vacated and remanded on Government's motion, 358 U. S. 915, dismissed, 172 F. Supp. 107], which expressly acknowledged that the protection of

(*Continued on page 380*)

*Presented before the Trademark Division; Section of Patent, Trademark and Copyright Law, American Bar Association, August 23, 1959.

STRUCTURE OF A PHARMACEUTICAL FIRM*

BY GEORGE W. ORR, JR. PRESIDENT AMES COMPANY, INC.

In doing the research that formed the basis of this presentation, perhaps the first thing that became apparent was the fact that there is no such thing as a typical pharmaceutical company. I suppose this is to be expected, because the modern business corporation is a creature of evolution and, in the case of pharmaceutical companies particularly, much of this evolution has been compressed into relatively few years due to the dynamic growth of our industry. It seems no more reasonable to expect to find a typical pharmaceutical company than it is to expect to find a typical mammal, although, like the former, the latter have certain common structures and systems.

Definitions

In order to establish communication, I must make a few definitions. A great deal of time has been spent arguing over definitions of "line" and "staff." I shall define them in what I consider the most generally accepted way, so you will know how I use these terms, even though you may not agree with my definitions. "Line," then, is an activity that directly accomplishes the objectives of the organization, and "staff," an activity that provides advice and service to the line.

Line Varies

Since line is defined in relation to the objectives of the organization, it naturally follows that it will vary from one company to another, depending upon what that organization is designed to accomplish. Normally, in most textbook examples, manufacturing and selling are line. This is because these two activities are the principal ones of a great many companies. Staff, then, includes certain areas of financial management, legal counsel, personnel relations, research and development, and the like. These are usually referred to as service departments.

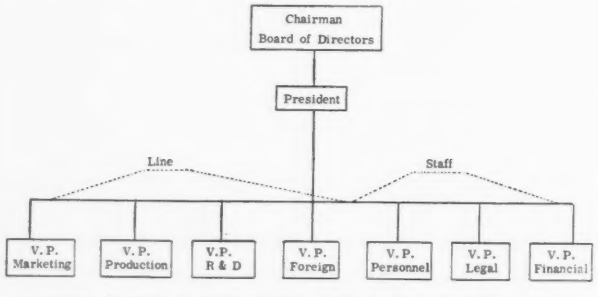


Figure 1. Medium-sized company without diversified interests.

However, in an insurance company, for example, selling and investing (financial management) are line activities, because these are the two principal activities that accomplish the objectives of the company. Similarly, in a law firm, legal service is line, and in a dry cleaning business, selling and service are the line functions.

Line within Staff

Each staff department in an organization has its own line, consisting of those individuals who carry out the principal function of the staff group. If the staff department is large enough, it may have its own internal staff as well. For example, a personnel department has people who interview applicants, counsel employees, and recommend sound personnel practices to other departments. These are line employees, because they carry out the department's principal functions; however, the personnel department may have its own specialists on testing methods or a trainer of interviewers and counselors. Such people would constitute staff, since they exist to serve the department's line.

Staff within Line

Most line departments have their own internal staff, and the more decentralized a company becomes the more staff people tend to become assigned directly to specific line departments, rather than exercising their function at the top corporate level. Some examples of staff within a line department are engineers in a production department and market research men in a sales department. These people do not directly accomplish the objectives of the organization, but specifically serve those within the department who are charged with this responsibility.

In my opinion, most pharmaceutical companies have three line operations— manufacturing, selling, and research and development. I do not expect general agreement on this from the pharmaceutical industry at large, because most of us have tended to think only of manufacturing and selling as line operations in the pharmaceutical business. However,

*Presented before the Pharmacy Education Industry Forum, August 1959.

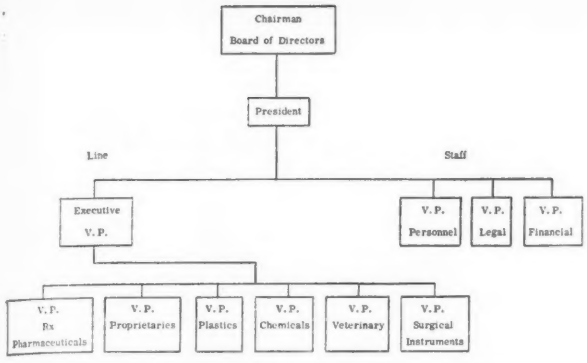


Figure 2. A complex, highly diversified organization.

I do feel that there is growing awareness of this "three-line" concept and, as we look at the historical development of pharmaceutical companies, I believe you will see why.

How Pharmaceutical Companies Grew

Most of the older pharmaceutical houses go back to the retail pharmacy. Merrell, Lilly, McNeil, and many others can be cited as examples. They became manufacturing pharmacists in the first place, by supplying the needs of physicians in the area for medicines for their patients. Many of these early manufacturing pharmacists were importers as well as manufacturers, for the need for medicines was great and they set out to fulfill this need in a particular area.

After these early manufacturing pharmacists acquired buildings and equipment to produce drugs, they began to reach out for business, so as to keep their facilities busy and their overhead under control. Thus, the drug salesman came into existence—the prototype of today's detailman or professional service representative. And thus, the second line operation, selling, became established.

Research and development has been identified as a function of the pharmaceutical industry for so long that it is a little difficult to determine just when it became a primary function alongside manufacturing and selling. While there was frantic research effort during World War I to develop replacements for drugs that had been wholly imported and were not available in this country, such as arsenicals, in my opinion it was not until the late 1930's that research and development began to emerge as a prime function of the pharmaceutical company, and that this was the result not of scarcity but of plenty.

To say it another way, it was the result of competition. By this time, there was much too much available production capacity for the established USP and NF drugs, and the industry had turned to the development of specialty products. While the early specialties were mostly established combinations of drugs in common usage by physicians, this list was becoming exhausted and competition for the doctor's specification was so keen that it became necessary to develop new therapeutic entities that contributed genuinely to medical practice in order to have a successful marketing program. These new products, of course, are now the principal medication doctors prescribe and use, and today a pharmaceutical house that is unable to compete on this basis simply cannot exist.

As a consequence, the development of new and better pharmaceutical agents has to be a principal objective of the pharmaceutical company because, unless this objective is met, the other principal objectives of manufacturing and selling will not be met. Therefore, by our definition, research and development is a line operation.

Examples of Basic Structures

While I warned in my opening statement that I could not show you a typical pharmaceutical firm, we can divide these companies into certain general classifications. Figures 1, 2, and 3 typify these basic structures.

Figure 1 shows what a medium-sized pharmaceutical company without diversified interests might be expected to look like. This is an example of functional grouping, that is, each principal function of the company is put in charge of one man who reports directly to the chief operating officer. This company we would refer to as being centralized, rather than decentralized, which permits most efficient operation in the smaller firm. When we begin to decentralize we have to start duplicating staff, and this is expensive.

You will note that we have provided only three staff departments at the top level here, although each of the line departments will undoubtedly include staff members who are concerned only with the operations of that line department.

Note that the foreign department is a line operation here, although I did not include it in my original enumeration of line departments. This is because the foreign operation is a mixture of production and marketing and, in some companies, includes research and development. Until comparatively recently, most foreign departments were called export departments,

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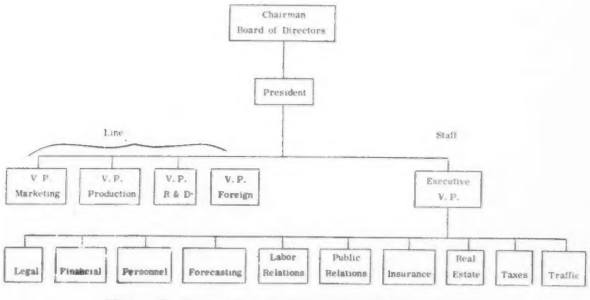


Figure 3. A very large, non-diversified company.

HAND LOTIONS AND CREAMS

BY JOSEPH KALISH, PH.D.

Approximately $50 million is now being spent annually by consumers for hand lotions and hand creams. Hand creams account for between one-fourth and one-fifth of the total, the rest being hand lotion sales. Surveys, for what they are worth, indicate that in each category about half of the sales are divided between two manufacturers, with the remainder of the market fragmented among all others.

Good Housekeeping asked of its readers the question that should be of primary interest to formulators of these products: "What qualities in a hand lotion or hand cream are most important to you?" For the six qualities mentioned, the order of importance for hand lotions was (1) effectiveness against roughness; (2) non-sticky; (3) quick drying; (4) effectiveness against detergents; (5) pleasant odor; and (6) consistency. For hand creams, requirements were very similar: (1) effectiveness against roughness; (2) non-sticky; (3) effectiveness against detergents; (4) quick drying; (5) pleasant odor; and (6) consistency.

Some of these preferences must be qualified by experience. It may well be that consistency, for example, is not important because the range has been limited by the formulator. The lotion must be thin enough to pour from a medium or small-neck bottle, but not so thin that it is watery and will run off the hands; the cream must be hard enough to be a cream and not a thick lotion, but must be soft enough to be easily spread on the hands. The consumer, in short, is little concerned with consistency, because she rarely encounters a product that is extreme in this respect. Perhaps the choice of lotions over cream is an indirect vote for the product with a consistency that permits flowing. Even more so, is what might be almost axiomatic in perfuming cosmetics, that odor preference is often a subjective reaction resulting in preference for some product as a whole without direct awareness that perfume influenced choice.

Consumer preferences are an excellent basis upon which to build a product; satisfy these first as much as possible and then add the packaging and formulation gadgetry for additional competitive advantage. Not surprisingly, the consumer first wants a hand lotion or cream to perform, to relieve hand roughness and overcome the effect of detergents on the skin. The film left on the skin should contain ingredients serving these purposes.

The effect of "harsh detergents" is partly a product of the competitive copy writer's imagination, since a number of reports in the dermatological literature indicate that the surfactant itself is no more deleterious to the skin than an ordinarily good soap. Heavy duty detergents, however, with alkaline boosters, do have some adverse action because they affect the normal acidity of the skin. An important value in a hand lotion or cream, then, would be the ability to restore normal *p*H values to the skin surface. It is not sufficient for the preparation to have a *p*H value between 4 and 6; it must have additional buffering power to neutralize the alkalinity caused by soaps and alkalies. Boric acid is almost ideally suited for this purpose except in instances where it is incompatible with other components.

Prolonged immersion of hands in surfactant and soap solutions will result in some loss of protective lipids from the skin surface and these should be

COURTESY ELIZABETH ARDEN

replaced by means of a fatty emollient. The choice here is very wide, embracing lanolin and its derivatives, lecithin and phospholipids, hydrocarbons, fatty acids, fatty alcohols, fatty acid esters, and fatty alcohol ethers.

A possible factor in the roughness of hands is that they may be immersed in water and surfactants long enough to cause loss of surface oil, and the cutaneous tissues may become partially water-logged. Rapid loss of this excess water, with consequent shrinking of the skin, can cause roughness and even cracking. An emollient here serves the additional purpose of regulating the loss of moisture from the skin. By "occluding" the surface, the oily layer retards loss of water vapor and minimizes shrinkage. This is especially true when the skin has not undergone excessive soaking in water.

For emollient and moisture retention by the skin, lanolin is a most useful product, but it occasionally creates problems in emulsification and, used in excess, will leave a sticky film. Modified lanolins, liquid lanolins, and lanolin absorption bases are less likely to cause these problems. Rare sensitivity to lanolin is said to be avoided by the use of the acetylated derivative which has the further advantage of being water-repellant. The sterol content of lanolin, long touted as having specific value for the skin, may be useful in maintaining a complex emulsion system on the skin surface for normal skin function. Lecithin is also an emollient and emulsifying agent, but here again, excessive proportions cause stickiness. Mineral oil, petrolatum, and related hydrocarbons assist in creating an emulsion that applies smoothly and has occlusive moisturizing properties; the residual film will be oily, however, if too much of these hydrocarbons is present. Fatty acids, the commercial stearic acids with varying proportions of palmitic acid, are usually selected for their emulsifying properties (along with their respective soaps), but have a definite emollient and smoothing action on the skin. Fatty acid monoglycerides, again primarily selected as emulsifiers, are effective emollients. The oily fatty acid esters, butyl stearate, isopropyl palmitate and myristate, are much more fluid than usual vegetable oils and leave a thin protective coating on the skin.

Special and separate mention must be made of silicones, cetyl alcohol, and quaternary emulsifying agents, because of their value in hand preparations and, in fact, general skin treatment products. Cetyl alcohol, for example, is almost unique in the smooth, mat, velvety effect it imparts to cosmetic films on the skin. Silicone also imparts a special smoothness combined with a degree of water repellancy to the skin surface. Cationic emulsifying agents, other than their ability to make acid-stable emulsions and their antibacterial action, are substantive to the skin and leave it feeling very smooth. With better understanding of factors in emulsion stability, gums are not required in most formulations to assist in preparing a stable hand lotion; some of them, especially quince seed mucilage, impart silky smoothness to the skin and are often advantageous in lotions for this reason.

Allantoin as a debridement agent and in possibly promoting healing, seems a useful addition to hand lotions to assist in preventing and overcoming skin

(*Continued on page 416*)

RAYMOND FAGAN

SCHERING'S PUBLIC RELATIONS

BY TED KLEIN PAUL KLEMTNER & COMPANY, INC.

To a cattleman, every ounce of beef on the hoof means that many more dollars in his pocket when he sells his herd. And a lot of beef men know about the Bloomfield, N. J., pharmaceutical company headed by Francis C. Brown, because Schering's tranquilizer, Trilafon, has been used in recent years to keep more beef on their cattle.

Promoting an unusual use for a new product to a group that heartily resists being "sold" took a great deal of planning and a few headaches in the process. Along with the advertising department, Schering's public relations department was called into the marketing meetings to help solve the difficulties. The job fell to Ray Fagan, now acting director of public relations for the company.

Months before the new indication for Trilafon received Federal Drug Administration clearance, Fagan met weekly with the veterinary marketing team, and finally he and veterinary advertising manager, Jack Smith, began to formulate their combined public relations-advertising program.

Basically the problem was reduced to three essentials: (1) the product was to be sold only through veterinarians, but, (2) the concept of tranquilizers had to be sold to farmers and stockmen, and (3) they also had to be encouraged to see a veterinarian for details of Trilafon.

The solution to the problem, although simply stated, took some time to prepare. It was decided to use the "mountain stream" approach, that is, to carry pails of information to the top of the hill and let it trickle down to the bottom, wetting everything along the way. Groups of opinion molders were selected for the first effort. For one week after FDA clearance, advertising and public relations concentrated on informing veterinarians. Concering ethical products, the professional man must always be informed first, is the approach followed faithfully throughout the veterinary promotion program. After the veterinarians were informed, press briefings were held in Washington, D. C., and in Chicago for farm and agricultural experts, farm press specialists, livestock specialists, national farm and livestock representatives, and members of the U. S. Department of Agriculture.

Simultaneously, press and wire publicity was sent out. Specific farm publications received detailed data on the new product uses. Most of this material was prepared prior to the first release on the product, since Schering's public relations department has access to the clinical and laboratory departments and research reports, and works with their personnel.

More than is done in much product promotion, the public relations and advertising campaigns were based on an educational approach, to assist the veterinarian in selling the concept of tranquilization in cattle to prevent such occurrences as weight losses and shipping fever.

The effectiveness of the combined campaigns was difficult to measure. The internal success resulted in the cooperation of research and veterinary medical personnel who were solicited for speaking engagements at national meetings of livestock and agricultural teaching groups. They were also actively involved in preparing radio recordings, special educational aids, films, and the like.

The combined effort of all departments succeeded in establishing Trilafon as the leading product for these uses in 1958. Sales estimates based on trade opinion place Schering's Trilafon in veterinary markets at about $1,000,000 a year.

From the standpoint of the cattlemen, the results and advantages are difficult to measure, but reliable estimates place their normal annual losses at about $100,000,000 from shipping fever, weight loss, and other conditions that can be treated by Trilafon.

Schering's PR department doesn't limit its activities to the veterinary, which, in fact, receives a small percentage of PR time. Reporting directly to President Brown, the department currently consists of Fagan, Sam Convissor and Al Varian, plus two secretaries. Varian now handles veterinary promotion.

Activities for the department include all corporate public relations, which involve preparing financial and annual reports to stockholders, preparing and conducting professional symposia such as the six symposia held in the veterinary area, international public relations, all publicity, plus a variety of institutional projects.

To supplement and counsel the department, the PR firm of Edward Gottlieb and Associates is employed. Counseling involves all corporate public relations activities, with the exception of those in the financial area, for which the firm of Selvage and Lee is utilized.

The internal department works closely with the professional and trade relations activities headed by George C. Straayer, particularly in the preparation and carrying out of the company's continuing pharmacy programs. Special emphasis is placed on the annual National Pharmacy Week, for which the two departments join forces for a special promotion. This is handled in public relations by Sam Convissor.

Schering has devoted considerable attention to the sponsorship of professional symposia for physicians, veterinarians, and other allied groups—in keeping with the educational character of the firm's promotional programs. These meetings are organized to provide the busy practitioners with up-to-date, yet condensed, reviews of the most advanced information on therapeutic approaches to certain diseases.

Schering has sponsored the Geriatrics Symposium, with discussions centered on the care of the aged, and veterinary symposia on the use of tranquilizers in pets. Symposia costs range from $1,000 to $18,000, depending on location, number of speakers, and the number of guests invited.

Another highlight of Schering's public relations program has been the World of Medicine educational-TV series. These films—13- to 30-minute kinescopes—cost $75,000. Produced in the educational TV studios of WTTW in Chicago, they range in content from the etiology of peptic ulcer to the treat-

(*Continued on page 396*)

SAMUEL M. CONVISSOR

DIURETICS AND EDEMA

BY BERNARD IDSON, PH.D. RESEARCH DIRECTOR, JULIUS SCHMID, INC.

The Market

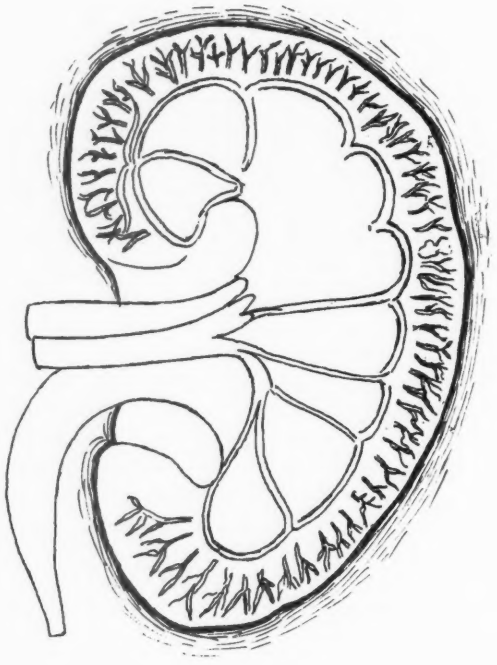
The relief of swelling of the tissues by excess water and electrolytes is a major medical concern. The diuretics used for the relief of this edema rank tenth in all prescription writings, accounting for about 5 per cent of all prescriptions, with general practitioners writing about 80 per cent of all the prescriptions. In the last year and a half there has been a radical shift in the popularity lineup of this $50 million market. Since the introduction of Merck's Diuril in late 1957, chlorothiazides have accounted for the largest share of the diuretic market. With the advent of Merck's, Ciba's, and Abbot's hydrochlorothiazides, Hydrodiuril, Esidrix and Oretic, respectively, it is expected that this segment of the diuretic market will account for an increased share of total sales in this area. The full significance of this shift within the diuretic markets becomes more pronounced when a study of past data is undertaken.

In 1957, total sales for all diuretic products was approximately $21 million. Fourteen million of this total was accounted for by new and refilled drug store prescriptions, the remainder achieved through government, hospital, industrial and armed forces sales. The leading product class in 1957 was the carbonic anhydrase inhibitors, of which Lederle's Diamox alone enjoyed sales of approximately seven million dollars. Xanthines, mercurials and aminouracil derivatives comprised the rest of the market.

The introduction of Diuril effected a sharp change in past patterns for all diuretic products. Diuril sales are derived from both the diuretic and hypertension markets. The approximately 15 million dollars total sales in 1957 can be attributed mainly to the diuretic market, since a great portion of its anti-hypertensive sales can also, directly or indirectly, be assigned to the diuresis desired in reducing fluid retention in the antihypertensive patient.

Total Diuril sales in 1958 were over 35 million dollars, or an increase of over 14 million dollars over 1957. In the first four months of 1959 drug store prescription sales were about 7 million dollars. Sales appear to have leveled, and may be expected to decline in light of the entrance of the hydrochlorothiazides. These have a combined sale of about 10 million dollars for the January-April 1959 period, and should reach over 40 million dollars for the year.

Diamox, the previous leader in the diuretic field, has settled down to a position of secondary importance. Its 1959 sales are expected to be about 3 million dollars. Xanthines, which did about 5 million dollars in 1958 are expected to decline to about 2-3 million dollars this year. Mercurials and pyrimides with sales of 3 million dollars in 1958 will fall below one million dollars in 1959.



Why this great demand for diuretics? What is edema? Which agents do what? How do they work? What's going on in other laboratories? What will future diuretics do?

Edema

The human organism carries 70 per cent of its weight as water. Loss of 20 to 25 per cent will usually kill. An efficient mechanism to balance water intake and excretion is maintained chiefly by the kidney. When this balance shifts and fluid infiltrates into the tissues, edema results.

Edema or dropsy is one of the most commonplace, yet extraordinary events in human biology. Why an organism should find it necessary to enlarge itself with brine is far from clear. Edema is rarely traceable to a single cause, for the factors are numerous and often from a vicious circle. Whatever the physiologic background, edema is a symptom of grave chemical and mechanical alteration in the cardiovascular-lymphatic system. The principal chemical alterations

are those which lower the effective osmotic pressure of the plasma or raise that of tissue fluid. The several mechanical changes that lead to edema formation are obstructions of either venous or lymphatic flow to produce adverse effects on capillary or lymphatic hydrostatic pressure. These changes place a functional burden on the body, for edematous tissue is ill prepared to assume extra loads as in healing of wounds or dealing with infection. Actually, in infection, if the diffusion of native fluids is interfered with by edema, so is that of any therapeutic agent which might be employed. Likewise, an addition to the volume of an administered drug will produce unexpectedly low ambient drug concentrations. Thus, it is obvious that attempts should be made to reduce edema wherever and whenever it forms, unless important contraindications such as active inflammation, exists.

The physiology of edema is quite abscure, yet it is generally accepted as due to an inability of the kidneys to excrete water and electrolytes. The kidney is concerned chiefly with the excretion of water-soluble metabolic products and controlling the concentration of the constituents of most of the body fluids. The formation of urine from blood occurs in the kidney as a two-step process, a glomerular filtration and tubular reabsorption. The glomerulus is a network of capillaries from which fluid filters. The glomerular filtrate contains all the crystalloids normally present in the blood but none of the cellular or protein constituents. As this dialyzate passes along the renal tubules approximately 99 per cent of the water and salts are reabsorbed into the blood stream to be made available for use by the body. The 1 per cent of the glomerular filtrate which is not reabsorbed by the renal tubule makes up the urine in a total volume of about 1.5 liters per day for a normal adult. The control of concentration of body fluids, particularly electrolytes, is the kidney's other great major function. When body abnormalities occur, upsets of anionic-cationic electrolyte balance occur, with subsequent shift of body fluid. A loss of certain ions, and retention of other ions, chiefly sodium, occur resulting in edema. The physician's main concern is to relieve the edema by promoting the excretion of water as urine through the use of diuretics.

Edema is found in a wide variety of disorders. Until the advent of recent potent oral diuretics the treatment of edema was limited to congestive heart failure or cirrhosis. Treatment has now extended to normal and toxemia pregnancy, epilepsy, premenstrual tension, obesity, glaucoma, nephritis, nephrosis and others. In congestive heart failure, the heart is unable to maintain a satisfactory circulation, rendering the kidney incapable of properly excreting salts and fluids, causing accumulation of fluid in the lungs or other tissues of the body. Digitalis is used primarily to increase cardiac output to improve renal blood flow and glomerular filtration rate. The study of the edema of toxemia of pregnancy has indicated significantly less excretion of sodium and chloride than in normal pregnant patients. In normal pregnancy edema, the water and electrolyte retentions may be secondary to high plasma levels of steroid hormones. The influence of various steroids is involved in the edema of premenstrual tension, where best treatment results by controlling salt and water retention with diuretics.

The aim of edema therapy is to achieve sodium balance without excessive retention of sodium, with consequent increase in the urinary excretion. Physiologically, this ideal can be accomplished by increasing renal blood flow and glomerular filtration rate and depressing tubular reabsorption of sodium. Diuretics hoping to accomplish this may be divided into three groups according to their site of action. First are those that act peripherally on the tissues to mobilize salt and water stored in cellular and extracellular depots. Those which act on the kidneys to inhibit water and electrolyte reabsorption are second. The last are those which act on the cardiovascular system to improve circulatory dynamics and the elimination of fluids from the body. Actually, the majority of the true diuretic agents act on the kidneys by one or more mechanisms, thus inhibiting water and electrolyte reabsorption and increasing its elimination as urine.

Osmotic Diuretics

The first great group of diuretics are those which alter the osmotic pressure of the serum and thereby promote diffusion through the kidney glomerular and tubular membranes. Water, hypertonic saline, glucose, sucrose, urea, sodium sulfate, sodium phosphate, and ammonium chloride are included. Theoretically, all the foregoing act by the same mechanism. The administration of a foreign substance or a normal urinary constituent in a concentration higher than that in which it can be eliminated from the body results in abstraction of fluid from the tissues, excretion of such substance in the urine, and finally osmotic diuresis. The increase in urine flow results both from the abstraction of body fluid caused by the osmotic pressure of the plasma, and reduction of the amount of water reabsorbed by the kidney as a result of the increase in the osmotic pressure of the tubular fluid exerted by the unabsorbed solute.

Water diuresis usually results from the ingestion of water or from the parenteral administration of isotonic solutions. Following its ingestion, water is rapidly absorbed through the intestines and distributed throughout the body. However, the absorption of water proceeds at a faster rate than urinary excretion. Urine flow usually begins to increase within fifteen to twenty minutes after water ingestion, reaches a peak within 60 to 90 minutes and returns to normal within 2 to 3 hours. Parenteral administration

(Continued on page 396)

RADIATION STERILIZATION

BY MORTON W. SCOTT AND ERNEST J. HENLEY, PH.D.*

The bactericidal and sterilizing properties of ionizing radiations were recognized shortly after the discovery of X rays by Roentgen in 1895. However, only recently, with the development of particle accelerators and nuclear reactors, have the pharmaceutical applications of radiation sterilization become intriguing commercial realities. Why is this radically different means of sterilization of such tremendous interest; and what are its future potentials?

Radiation sterilization is a process in which microorganisms are destroyed by exposure to streams of high-speed electrons, gamma rays, or other "ionizing" radiations. The sterilization is accomplished without a substantial rise in the temperature of the product, and in the usual application no radio-activity is induced in the treated material. Since radiation sterilization is essentially a heatless process, it appears particularly attractive for the sterilization of thermolabile pharmaceuticals and medical specialities. In addition radiation can accomplish sterilization of the product in its final container after all other packaging operations are completed. Chances of recontamination, then, are greatly reduced, and considerable production line savings may eventually be realized.

The application of radiation sterilization techniques to drugs and pharmaceuticals was suggested very soon after the general procedure began to receive substantial attention in the technical literature. Radiation sterilization has several important advantages. The technique may be used with an extremely wide variety of liquid, solid and semi-solid pharmaceutical products and with medical and surgical supplies. The heaviest radiation dose usually required for sterilization produces a temperature rise in the product of only about eight degrees Fahrenheit. Thus, this method is especially attractive in sterilizing heat labile substances.

Many therapeutic agents have been successfully sterilized with radiation. The list includes steroid preparations of estradiol, testosterone, and pituitary hormone; antibiotics such as penicillin and streptomycin; and other materials such as protein hydrolysates, novocaine, and ephedrine. In all of these cases, no loss in activity was observed after processing and no toxic or other deleterious effects were produced. The impression should not be left, however, that radiation sterilization is a completely innocuous procedure. Many substances such as ascorbic acid and insulin are inactivated by radiation exposure. In addition, the possibility of forming toxic by-products is always present, although there have been no such cases reported.

Another advantage of radiation techniques lies in the fact that products may be sterilized directly in their final sealed containers. In this way, the possibilities of bacterial recontamination are greatly reduced. The need for sterile filling schemes and costly aseptic procedures is also removed.

A number of pharmaceutical products are currently being processed by radiation. These include sterile enzyme preparations (Johnson and Johnson) and sterile surgical sutures (Ethicon Inc.). Radiation-sterilized polyethylene tubing suitable for surgical use has been placed on the market by Clay-Adams Inc.

Successful sterilization of human aortae for subsequent transplant into patients suffering from coarctation of the aorta has been achieved. These studies indicate great potentialities for sterilizing other types of tissue by use of ionizing radiations.

The inactivation of viruses, including polio, by radiation may also show promise. Radiation seems to inactivate the nucleic acid strands in virus, but does not degrade the protein. Inactivated virus thus retains its natural configuration, which is necessary for antibody production. The radiation treatment is much more selective and controllable than the usual formaldehyde processes. Rabies and rat polio vaccines prepared with radiation show the same potencies as those for formaldehyde-treated material but are, as was expected, far more consistent.

The radiation sterilization of cotton products such as gauze pads, bandages and similar products is currently under study. It is likely that in the near future materials treated in this way will reach the market.

Of course, a great deal of work is concentrated in the food preservation field. Such things as meat, vegetables, fish, fruit and cereals have already been processed. With grains, major emphasis has been placed on insect deinfestation procedures. With potatoes, the application seems to be in the field of sprout inhibition. Toxicity studies, animal and human feeding tests, and acceptability tests have been completed with almost all of these products.

Problems of Radiation Sterilization

While studies on the bactericidal effects of radiation have led to a point where some degree of predic-

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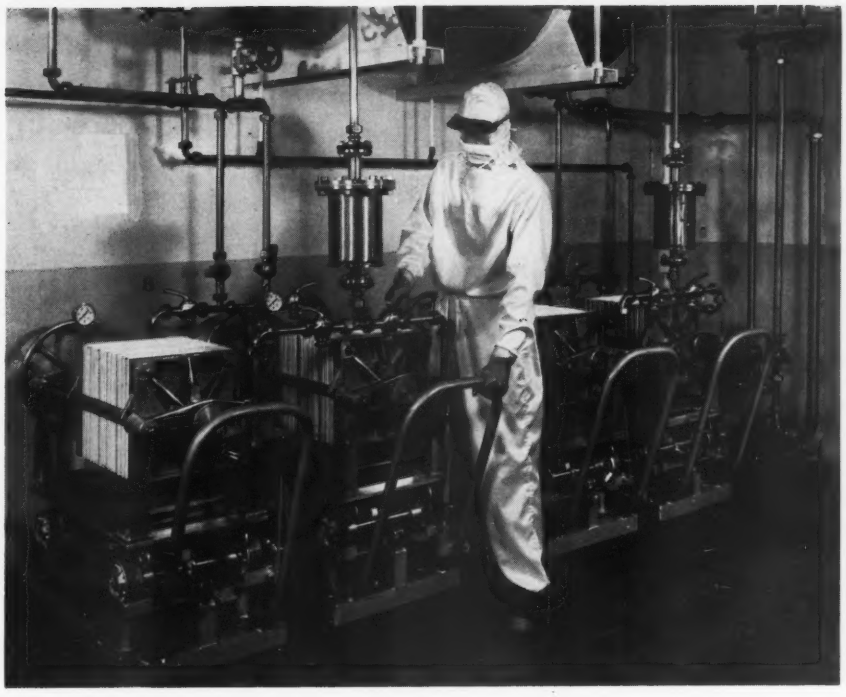

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tability can be attained, the suitability of radiation sterilization for many types of pharmaceuticals is still open to numerous questions. Perhaps the most serious problem arises because ionizing radiations can react with all forms of matter, and their effect is not limited to microorganisms alone. Like heat sterilization procedures, radiation treatments may often induce undesirable changes in both the product and the packaging materials. Unlike thermal processes however, these changes may be quite subtle, so that their detection may require a full program of testing and evaluation.

The reactions caused by ionizing radiations in even the simplest chemical systems are complex, and, in many cases, the end-products are unpredictable. These reactions occur because the radiant energy (required for sterilization) is generaly sufficient to break a small percentage of the chemical bonds present in the treated sample. New compounds and/or reactive species are thereby generated within the product. For example, uronic acid has been isolated from irradiated solutions of glucose (and other hexoses) and pyruvates can be detected in irradiated samples of lactic acid.

With pharmaceutical systems the side reactions caused by radiation may be very troublesome. They may lead, for example, to a reduction in therapeutic activity, reduced product stability, or to the formation of toxic by-products. Undesirable organoleptic changes may occur also. This last point has introduced considerable difficulties in the development of food irradiation procedures (particularly with meats and fish).

The Food and Drug Administration has naturally approached the subject of radiation sterilization with a great deal of conservatism. In the past, this agency considered pharmaceuticals sterilized by radiation to be "new drugs" requiring new drug applications. This restriction imposes no hardship with new products in the early phases of their development. However, for many products already on the market, it is unlikely that radiation processing will be substituted for the existing sterilizing techniques, because of the cost and difficulty in obtaining new drug approval.

It is also of interest to note that radiation sterilization—in the sense of loss in viability of the microbiological population—does not insure cessation of enzyme activities of the contaminating organisms. For example, it has been shown that some bacterial and other enzymes systems may be highly radiation-resistant and continue to show activity long after viability has been destroyed. Radiation doses in excess of 5 million roentgens may be required to destroy these enzymes. This situation is not at all like that experienced in heat sterilization procedures where the elimination of enzyme activity coincides with, or actually preceeds, the loss of viability.

The problem of enzyme functions in radiation-sterilized pharmaceuticals gains importance because residual enzymatic reactions may cause many undesirable changes in "sterilized" pharmaceuticals. To preserve adequately drug materials that can act as enzyme substrates, it will be necessary to collect not only viability data, as from plate counts, but also measures of residual enzyme activities. Of course,

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A NEW LOOK AT TABLET LUBRICANTS

BY W. A. STRICKLAND, JR., PH.D.

SCHOOL OF PHARMACY, UNIVERSITY OF ARKANSAS MEDICAL CENTER, LITTLE ROCK, ARKANSAS

Tablet makers are aware that granulations are usually not suitable for compression without the addition of small quantities of a "lubricant." The function of this additive is to enhance, in several aspects, the processing qualities of the granulation. In the past, materials tested and used as lubricants have been evaluated in a qualitative manner by observing the tablet machine in operation and the tablets being produced to see whether or not the process yielded acceptable tablets. By this empirical procedure many excellent tablet lubricants have been found and are widely used, among which are magnesium stearate and other metallic stearate soaps, stearic acid and mineral oil. Recently, precise methods for evaluating tablet lubricants have been evolved.[1,2] Some of the data derived from these studies will be presented in this article.

One difficulty encountered in studying and employing tablet lubricants is the loose definition of the term "tablet lubricant." For example, tablet lubricants have been defined as follows, "A lubricant is generally defined as a substance which is added to the granulation to insure uniform feeding into the die and to prevent the material from adhering to the punches and die during and after compression."[3] This definition implies that a tablet lubricant should promote granulation flow and act as an anti-adherent. Another author states, "The purposes for which lubricants are added are: (a) to assist ejection of the tablet from the die, (b) to prevent the tablet from sticking to the punches, (c) to give an attractive finish to the tablet."[4] Agreement appears to be common on the point that lubricants should prevent adherence of the tablet to the punches and die.

Research in this field[1] has demonstrated that the primary function of commonly used tablet lubricants is the reduction of friction that arises at the tablet-die wall interface during tablet formation and ejection. This is, in truth, lubrication, wherein small amounts of a suitable material are interposed between two rubbing surfaces, to reduce friction and wear at the interface.

During the course of the study of tablet lubricants[2] it became evident that the tablet maker deals with three distinct functions, namely, (a) lubrication in a true sense, (b) improvement of flow properties of granulations, and (c) anti-adherence to prevent picking and sticking on the punches as well as adherence to the die wall. This thinking was accentuated by the obvious contradictions found when considering magnesium stearate, for example, which is an excellent lubricant at the tablet-die wall interface yet

actually tends to retard the flow of granulations.[5] On the other hand, talc has been shown to be only moderately effective as a lubricant but it has been found to be an excellent anti-adherent and actively to promote granulation flow.

To take an enlightened approach to tablet formulation it is well to bear in mind these three functions, each of which will be discussed separately.

Lubrication

Lubricants, as has been previously stated, are materials interposed in small quantities between surfaces in relative motion in order to reduce friction and wear. The mechanism of lubrication has been elucidated for metal-metal and other systems[6] and is generally considered to occur by two mechanisms. The first is termed fluid (or hydrodynamic) lubrication because the two surfaces are separated by a finite and continuous layer of fluid lubricant, which under ideal conditions prevents wearing of the solid surfaces. Hydrocarbons, such as mineral oil, are examples of fluid-type lubricants. These lubricants have been shown to depend upon viscosity for their effectiveness in tablet manufacture.[7] They lubricate the die wall and prevent seizure of the two surfaces in proportion to their ability to maintain the continuous layer between the two opposing surfaces. If, for example, mineral oil is used at high punch pressures (around 20,000 p.s.i.) it would probably be ineffective, whereas the more viscous paraffin would probably prove to be an effective lubricant. At lower punch pressures (around 5,000 p.s.i.) mineral oil may be useful in some formulations.

Boundary lubrication, the second mechanism, results from the adherence of polar portions of molecules with long carbon chains to the opposing surfaces. Magnesium stearate and stearin acid are examples of boundary lubricants. This type lubricant is most commonly used in tablet manufacture because it is more effective, requires smaller quantities, and is more easily applied to granulations. The lubricating efficacy of boundary type lubricants is generally related to the carbon chain length of the dipolar molecules.

The following table is taken from a more extensive table compiled during the study of the relative effectiveness of tablet lubricants.[7] In this study 2 per cent lubricant was used throughout and the lubricant was added to the granulation in the form of 100 mesh or finer powders, except as noted by an asterisk which indicates that the lubricant was sprayed on tumbling granulation as a solution. The instrumented tablet machine was equipped with a ⅜ inch flat-faced steel punch and die set and the machine adjustments were essentially the same for all these determinations. The letter R indicates the ratio between the maximum lower punch force and the maximum upper punch force during compression. This has been found to be a convenient index of lubrication in this study; perfect lubrication would have a value of unity on this scale. The types of lubricants are designated as follows:

F—fluid type
B—boundary type
I—indefinite mechanism of action
A—anti-adherent
O—no apparent lubricant activity
?—lubricant mechanism questionable

Glidants

V. K. Munzel long used the term "lubricant" to describe materials that reduced friction during tablet compression as well as those agents which facilitated the flow of granulations. Recently,[8] he employed the term "glidant" to designate agents added in small amounts to improve flow characteristics of granulations. Addition of words to our technology is not to be taken lightly, but it may be justified in this case because, as previously pointed out, a true lubricant such as magnesium stearate retards granulation flow and may be termed a poor glidant. As a matter of fact, most lubricants, both boundary and fluid types, do not promote granulation flow; many tend to retard it.

Such materials as talc and the starches are examples of good glidants.

Anti-Adherents

The function of an anti-adherent is to prevent tablet material from sticking to the punch faces, and, to an extent, to the die wall. Anti-adherents have been studied extensively in several fields but little attention has been given them in tablet work. There is some overlapping between anti-adherents on the one hand and glidants and lubricants on the other; talc

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ESSENTIAL OILS ON REUNION ISLAND

BY ERNEST GUENTHER, PH.D. FRITZSCHE BROTHERS, INC.

Geranium fields in foreground of the volcanic highlands near Cilaos.

This tropical island, a French possession located roughly 400 miles east of Madagascar, is now the world's principal supplier of geranium oil and (next to Haiti in the West Indies) of vetiver oil. It also produces small quantities of ylang ylang oil.

Production of the oils of geranium and vetiver is a primitive industry, largely in the hands of descendants of early emigrants from France, who have stayed in the highlands of Reunion ever since their ancestors arrived in the late sevententh century. Clinging to their old language and customs, they have kept to themselves, enjoying almost no contact with the outside world. Avoiding intermarriage with the Negro slaves who were imported to work the sugar plantation in the coastal lowlands, these "hillbillies" have kept their race fairly pure. They are, perhaps, a bit inbred because of frequent intermarriage, but on the whole they seem a remarkably hardy lot, able to withstand the frequent frosts in these high altitudes without adequate housing and clothing. Their poverty is appalling: living in thatched huts and dressed in thin cotton material, without shoes and overcoats, they wring a scant livelihood from the soil, growing geranium and vetiver by obsolete methods, working as sharecroppers endlessly indebted to the landlords. This is "tobacco road" at its worst, with no advance in generations. Nothing has changed in these peoples' ways of living—so it seems to the visitor—since their forebears first came over from France.

Conditions are much better in the coastal lowlands where sugar cane is grown extensively. The powerful sugar industry, with its government-supported prices, is in a position to finance the purchase of land for the growing of cane, to absorb the crop at profitable prices, and to offer steady employment at decent wages. It is quite obvious that the essential oil producers, unorganized, and plagued with all sorts of agricultural and commercial hazards, cannot compete with the sugar industry. In fact, whenever sugar cane moves into a territory the essential oil producers will soon be driven out. Sugar cane requires little care and does not suffer much from cyclones—only 10 to 15 per cent being destroyed by even a severe storm. No wonder, then, that on Reunion Island land is planted with cane wherever possible, from the coast all the way up to altitudes where the terrain becomes so steep that the cane can no longer be trucked down to the refineries.

A main street in St. Denis. At right, St. Denis' leading hotel.

Essential oil-bearing plants, on the other hand, are much more difficult to raise. Geranium in particular is a very delicate plant, requiring a great deal of care and constant replacement of dead stocks. Cyclones may destroy the entire crop and actually blow away the planting. Strong winds will tear off leaves; heavy

rains may waterlog the soil, with resulting development of the dreaded "rouille," which kills the plant. Moreover, the prices for essential oils are liable to wide fluctuation, being governed not only by supply and demand, but also by speculation.

That production of oils of geranium and vetiver has been able to survive in Reunion, despite outmoded methods, must be attributed to these factors:

(1) In the altitudes where geranium and vetiver are cultivated the terrain is so rugged that practically no other crop can be raised.

(2) The population in the highlands is so poor that any crop, even the most hazardous, serves for a livelihood.

(3) The production of geranium, as well as of vetiver, is a family industry, in which every member of the family participates without being paid any wages.

(4) There is a traditional "know-how" among the highland people as regards the cultivation and distillation of these aromatic plants.

In brief, geranium oil production—and to a lesser extent that of vetiver oil—on Reunion Island is an industry that keeps the population of 4,000-5,000 wretched hillbillies alive—but only miserably so.

Oil of Geranium

Geranium grown on Reunion is considered to be botanically identical with the Algerian species, although soil and climate may have produced certain differences in quality and yield of oil.

On Reunion two types of geranium are cultivated (probably horticultural varieties of *Pelargonium graveolens*): the "white," sturdier and more resistent to moisture—this type has pinkish flowers; and the "red," which yields 50 to 60 per cent more oil—an oil of more pronounced and characteristic odor. This variety bears flowers of a slightly deeper color than the "white" geranium. Because of its higher oil content, and the superior quality of the oil, the "red" type of geranium is gradually replacing the "white" type.

Cutting geranium on Reunion Island.

Geranium is cultivated at altitudes ranging from 1,500 to 4,500 feet, and exclusively on the western and southern areas of the island, on slopes so steep that no other crop (except perhaps the potato) can be grown there. The soil here is largely decomposed volcanic, with deep humus. This rich soil may be responsible for the high quality and yield of Reunion geranium oil; no other area in the world enjoys so high a yield.

On Reunion the main rainy season begins in December and runs into April; but there are lesser rainfalls in other months. Annual precipitation reaches about 40 inches. In this connection, it appears possible that the high humidity typical of Reunion—a result of the Indian Ocean breezes that blow continuously over the island, even during the dry season—has a beneficial effect upon the growth of geranium; by contrast, in the highlands of Kenya and the Belgian Congo—where the dry season is prolonged and devoid of atmospheric moisture—the geranium plant becomes easily exhausted.

Replanting vetiver by division of the root stock.

Propagation of plants is done with cuttings. These are planted in the ground at the beginning of the dry season (May to July), or occasionally as late as August, while the ground is sufficiently moist. Har-

A typical field distillery of geranium on Reunion Island.

vesting of the new plants can take place in January. A field may last for twenty years with proper care: dead plants must be regularly replaced; the ground must be enriched with exhausted (i.e., the residue of distilled) plant material fermented for three months, and it should be provided with chemical fertilizers (8-16-16). Recent experience has shown that careful fertilizing can almost double the yield of oil per acre. However, proper treatment is not always possible; generally it is given only in periods of favorable prices for the oil.

On Reunion Island the geranium flowers only in

Harvesting the vetiver root—extraction from the ground.

September. Since a low yield of oil always accompanies the period of flowering, the plant is not cut in September. But for the rest of the year harvesting for distillation may go on continuously. There are, however, two peaks for cutting: the chief, or summer, harvest takes place from December to March—or even April—if sunny weather prevails; the lesser, or winter, harvest lasts from May to October (this smaller harvest yields about one-fourth of the total annual quantity of oil). Heavy rainfall is disastrous: one week's rain may destroy an entire crop; without sun, leaves turn from green to red, and the essential oil disappears.

Yearly production of geranium oil on Reunion Island is distributed as follows:

Summer harvest peak	40-50	metric tons
Winter harvest peak	15-20	" "
Intervening harvests	20-25	" "
Total	75-95	metric tons

Distillation of geranium plants is carried out in small units, of which there are several hundred on Reunion Island, processing the material from thousands of small plantings. A still holds about 250 kilograms of plant material, of which about two-thirds are branches and the remainder leaves. The stills are very simple, of metal, and easily transportable. Provided with a perforated grid to separate the plant charge from the boiling water beneath, they are heated by open fire; wood is brought from nearby forests, where possible. The landowner who owns his

Charging a typical vetiver still with root material on Reunion Island.

timber is thus at an advantage. Recently a somewhat improved type of still has been introduced, which saves fuel and gives a slightly higher yield of oil.

An old wine bottle serves generally as oil receiver. About three hours and some 150 pounds of wood—a high figure—are required for distillation of one charge.

Before distillation, the cut plant material may be left to lie and wither for about twelve hours in the field; this drying reduces the weight and volume of the material, and allows for closer packing in the still.

The yield of oil varies considerably with the age of the field, the care it has received, and with climatic and seasonal factors. Summer yields are generally higher than winter yields. Hot weather, particularly when a cyclone impends, produces the highest yields; rainy weather the lowest. Since distillers do not weigh their plant material before distillation, exact figures of yield cannot be calculated. However, experienced growers estimate that 1,000 pounds of plant material yield roughly 1¼ pounds of oil.

Quality of oil apparently varies with locality of production, although systematic comparative estimates have not been made. Government chemists, in the laboratories in St. Denis, and experts among the exporters, believe that the finest oils come from Tampon (Plaine des Cafres), with Chaloupe St. Leu and Trois Bassins following.

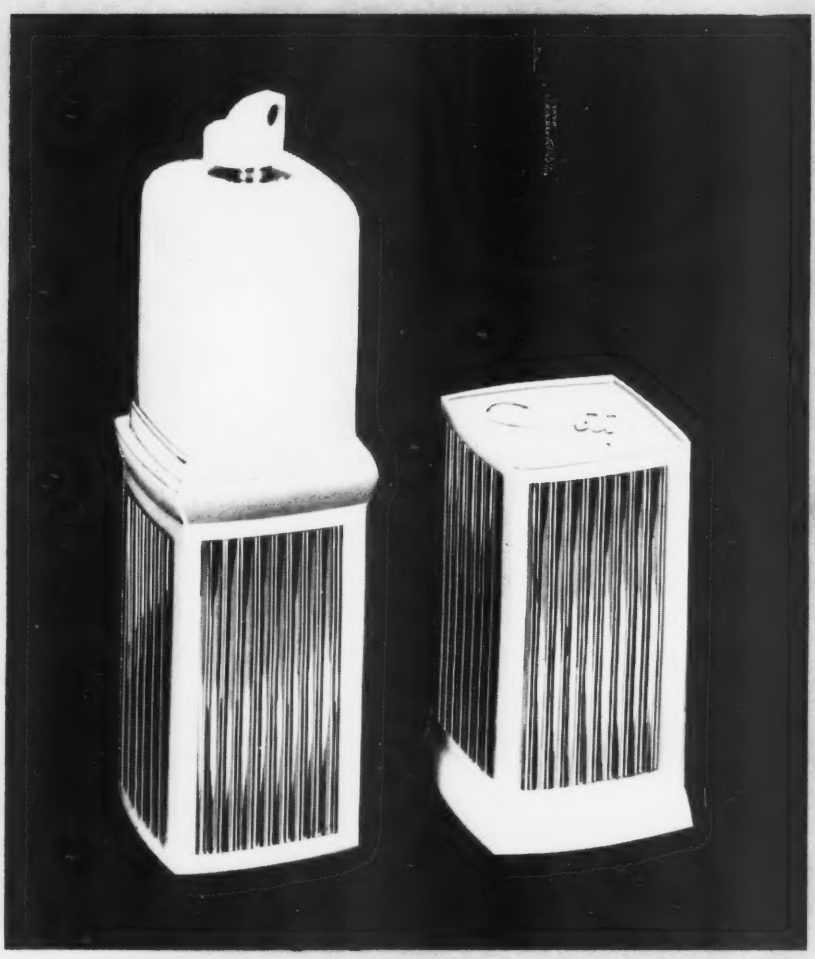
Official specifications for Reunion geranium oil follow:

Specific Gravity at 15° C.	0.888-0.897 (temperature correction factor 0.0008)
Optical Rotation at 20° C.	—7° to —13° (the laboratories accept only oils of —9° to —13°)
Refractive Index at 20° C.	1.4617 to 1.4660
Acid Number	Below 7
Ester Number	50 to 78
Ester Content (calculated as Geranyl Tiglate)	23 to 33%
Solubility (70% Alcohol)	1 vol. soluble in 1.70 to 2.0 vol.
Characteristics	Limpid, with no substance in suspension.

Practically all the oil reaching exporters in St. Denis arrives in small lots; these lots may have been

(*Continued on page 410*)

Packaging and Selling



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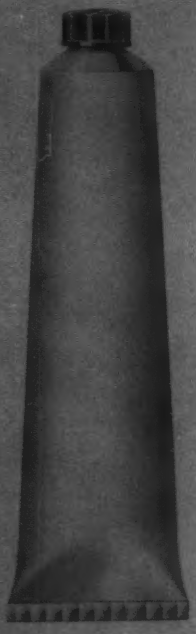

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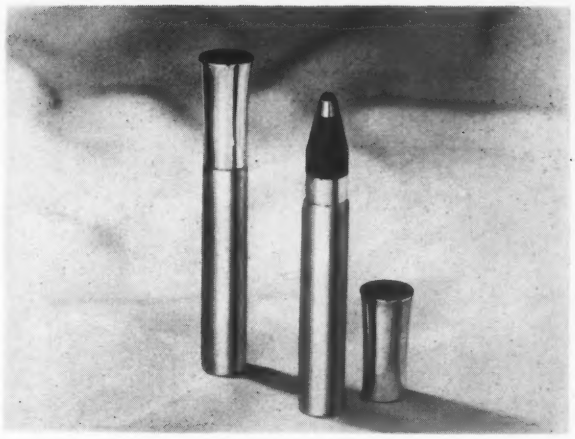

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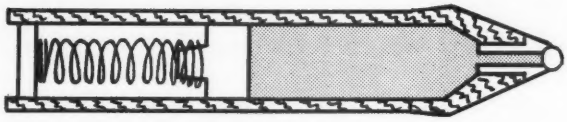


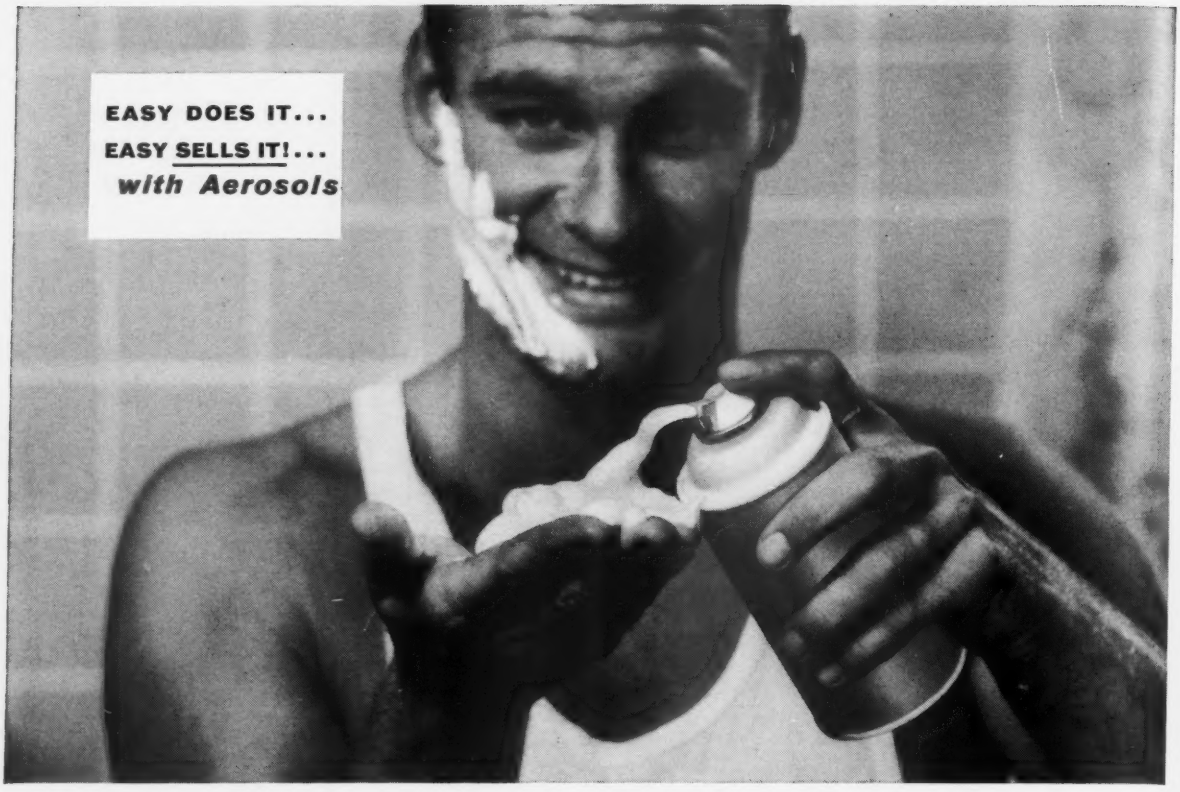
Richard Hudnut will go National in October, with the new "Lip Quick," a ball-point roll-on lipstick. This device will be given full promotional treatment in magazines, on the radio and television, and, if present indications are borne out, it may have a revolutionary effect on the lipstick market.

The stick is slimmer than others, to fit a woman's small hand, and possesses the obvious advantages of neither being breakable in use nor becoming soft and greasy in hot weather. With it, color can be sharply outlined on the lips, to replace lip liners and lip brushes; pressing the lips together after the outlining uniformly distributes color and mass. Because it requires no stiffening waxes, considerable latitude in the formulation of the mass can more readily result in a lip coating with the most desirable application, adherence, appearance and protective qualities.

The package is a model of simplicity. The metal case, which has a slip-on cap, holds the easily replaced refill. The refill, as shown in the drawing, is a black molded nylon cylinder, conical at one end. An insert in the tapered end is a small metal tube holding a glass ball with a special finish facilitating flow and discharge. The color mass behind the ball is held in place by a polyethylene piston kept under pressure by means of a spring. Regular feed of the mass is thus assured in any position, and the total amount corresponds roughly to about 50 per cent more than that of the average lipstick.

Hudnut is operating under a world-wide, exclusive license from the Omega Manufacturing Company of Inglewood, California, which developed the product and package and now manufactures and assembles "Lip Quick." The applicator has been tested and developed for more than three years, in West Coast beauty parlors, during which time inevitable "bugs" were removed. These included not only mechanical factors of constancy and dependability of feed, but also the development of a mass of exactly the correct consistency, that is, neither too thick nor too fluid. The present formulation applies easily and smoothly, without "feathering" and also without deposition in crevices.

Test marketing by Hudnut in Seattle, Kansas City, and Atlanta produced results that quickly led to the decision for national distribution. At present, eight shades are available, at a price of $1.50 for the simplest case and $1.25 for refills. •



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By majority vote at the cash register, most shavers agree: an aerosol shave is a faster, cleaner, easier shave! These advantages of pressurized shaving lathers sold over 50 million cans in 1958. They accounted for a greater dollar volume than the sales of *all* shaving creams, shaving soaps and shaving sticks combined!

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Contract Fillers—We will also be glad to put you in touch with highly capable contract fillers in all parts of the country who will put up your product in aerosol form for test marketing and handle full commercial production as well.

For further information—or if you would like to arrange for a special market presentation—write today to "Genetron" Dept., General Chemical Division, Allied Chemical Corporation.

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MARKETING PHARMACEUTICALS*

BY RICHARD L. HULL, SMITH KLINE & FRENCH LABORATORIES

It is fashionable today to speak of companies as being "market oriented" or as having adopted the "marketing concept." Where once there was a "sales manager," or a "vice-president in charge of sales," the tendency now is to have a "director of marketing" or a "vice-president for marketing." Perhaps the functions remain essentially the same, but the proponents of the new terminology visualize marketing as something much broader than sales. Let me illustrate this by quoting one definition of the marketing concept, a definition offered by Arthur P. Felton of the American Brake Shoe Company in the Summer issue of *The Harvard Business Review*. Mr. Felton says that the marketing concept is "a corporate state of mind that insists on the integration and coordination of all the marketing functions which, in turn, are welded with all other corporate functions, for the basic objective of producing maximum long range corporate profits." Elsewhere in his article he speaks of the importance of planning. Apparently what we need, then, is a form of organization and a state of mind which will lead to better market planning.

Incidentally, to do the best market planning, we need the best possible information about our markets —marketing research information, in other words. I shall discuss marketing research later.

Total acceptance of the marketing concept, or of marketing as the most dominant function in the pharmaceutical industry, could have many implications, and I am not sure that they are all desirable ones. I would be most concerned with the possibility of restricting or circumscribing basic research in our laboratories. However, the increased emphasis on marketing as a corporate activity is resulting in two developments which I consider highly desirable.

The first of these is better integration and coordination of our five traditional marketing functions: sales, advertising, distribution, public relations, and marketing research. Each complements all of the others, and we can no longer afford to let them go their separate ways. Coordination of the efforts, and budgets, of the five activities calls for planning, and this in turn becomes a sixth function in itself.

Thus, the first of these two developments is better planning of the marketing effort, better budgetary control, and improved team work. The concept of

a director of marketing, supported by a planning department or staff section, bringing order into a situation where chaos previously prevailed, is obviously an exaggeration of what is actually happening. We have seen, and will continue to see, an evolution rather than a revolution in the marketing function. That evolution can be expected to continue, and planning will be a more and more essential ingredient in pharmaceutical marketing.

The second of the two developments which I applaud is the increasingly closer relationship between the marketing function and new product planning. In defining the marketing concept, Mr. Felton spoke of welding the marketing functions with "all other corporate functions." In our industry, as in many others, the most important of these other corporate functions is the creation and development of new products. The greatest challenge which the marketing concept offers us is that of properly welding research and development on one hand, and marketing on the other. This can be very sticky business. As I have already indicated, I do not believe that marketing can or should control our research programs, yet marketing must have an important and influential voice in new product planning and new product development. The costs of getting a new product ready for the market are substantial, and are constantly increasing. If a potential new product is fully

*Presented before the Pharmacy Education Industry Forum, August 1959.

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developed and then not marketed, but rejected and put back on the shelf for commercial reasons, a serious waste of money and scientific effort results. On the other hand, if a new product is developed and marketed but becomes a commercial failure, the waste of money and effort is even more serious.

Any proposed new product should have its commercial potential appraised by marketing, even as its scientific and medical attributes are evaluated by the scientists in research and development. This should be a continuing process while the proposed product is still in the laboratory or in the clinic.

Here again, planning and coordination become necessary. If marketing should not dictate to or control the scientists in our laboratories, it is equally true that research and development must not assume control over marketing. To resolve possible conflicts, most companies have a new product planning function of some sort. It may be a department, a committee, or even a single individual, but it should function in such a way as to permit the scientist and the commercial man to meet on common ground. Perhaps I should say neutral ground. The important consideration here is that under the marketing concept the laboratories will not put a finished product in a bottle, unveil it before a sales manager, and say, "Here it is, take it out and sell it."

Even so, we are accused of introducing too many new products, which is usually a way of saying that we introduce too many products which fail to sell in any substantial volume. I will not attempt to defend our record of successes and failures, nor do I concede that it needs defending. However, I will readily concede that as long as any significant number of our new products do fail in the market place there is room, and need, for improvement of the record.

The great merchant, John Wanamaker, is supposed to have said that half of his advertising was wasted, and that he would happily eliminate it if he only knew which half. I suspect that by strict accounting standards half of the new pharmaceutical products which will reach the market in the next year may be failures. Unfortunately, like John Wanamaker, we do not know which half.

For every new product that does reach the market, there are many new compounds, or proposed new products, or product ideas that are killed or abandoned for one reason or another. In this weeding out process most of us have been guilty of colossal mistakes. I could offer some embarrassing confessions myself and I am sure that most readers could add to the list.

This is because there are still broad areas in which judgment must operate, and none of us is infallible in his judgments. One great challenge to our industry today is to narrow these areas for judgment, to provide better facts which will in turn provide a sounder basis for planning. This applies both to new product selection and planning and also to the marketing or promotion of products already on the market.

This brings me to the subject of marketing research, and, incidentally, to a brief discussion of some of the unique characteristics of our distribution system.

The first of these is found in the special relationship among the manufacturer, the pharmacist, the physician, and the patient. Our products are sold to the pharmacist, either directly or through wholesalers; they are promoted primarily to the physician, but they are actually purchased by the patient. As a result we sometimes seem uncertain as to just who our customer really is.

As far as the retail pharmacist is concerned, we must not underestimate his role in the distribution of our products, for those products must be readily available to the patient when and if demand is created. Neither must we overemphasize sales to the pharmacist under the mistaken idea that such sales are necessarily desirable ends in themselves. To have an adequate distribution is essential, but if filling the pipe lines means flooding the pharmacies, this is poor marketing practice. In the long run we gain nothing by overloading the pharmacist's shelves.

Perhaps it is most realistic to think of the prescribing physician as our customer, for the use of our products is almost entirely dependent on him, and, consequently, the great bulk of our marketing effort is directed toward him. In speaking of the prescribing physician, we are not usually drawing a distinction between the prescriber and the dispenser, for across the country dispensing is at an all-time low. Rather, we refer to the physician who, by the nature of his practice, has frequent occasions to prescribe drugs for his patients. These are primarily the ones in private practice, the general practitioners and selected specialists, including the internists, the obstetricians, the pediatricians, the surgeons, the dermatologists, and certain others.

There are perhaps 225,000 licensed physicians in the United States, including those who are retired and others not in active practice. Of this number, slightly more than half or about 125,000 fall into what I would call the "prescribing physician" category, although the number and the composition of the group varies according to the nature and use of the particular product being marketed. For example, the obstetrician is not a good prospect for a pediatric product, nor is the pediatrician a logical prospect for a hypotensive agent.

Thanks to the fact that physicians must be licensed, and because the American Medical Association maintains what has been called the best professional directory service in the world, we have accurate lists of physicians, together with good information on the nature of the individual doctor's practice and his specialty, if any. As more and more phy-

(*Continued on page 384*)

you have to
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into a
product
At Newman-Green we believe in the axiom of all true craftsmen. Quality cannot be inspected into a piece—it has to be built into the piece.
The aerosol manufacturing and sales policy based on product quality, service and honesty will always provide you with the best buy. This is just as true on the smallest orders as it is on the largest orders. Newman-Green customers are assured of this fine craftsmanship because our first concern is to provide you with the best product quality possible for the money spent. Call your Newman-Green representative today.

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Packaging and Selling

The ball-point or roll-on lipstick will be entering its fourth month in market testing by the time this issue appears. As of now, August 15th, we understand that this new Richard Hudnut lipstick has been on the market for three weeks and has been under test in a few West Coast cities.

We hear that this test was very satisfactory in one large chain, with several repeat orders less than one week apart. At the same time, the sale in a department store in this city was not so satisfactory.

It is said that the company has plunged pretty heavily with its new lipstick, in an effort to find a leading specialty for the division that can pull it into the mass market and sustain heavy consumer advertising, particularly radio and television.

Not long after introduction of the ball point pen this trade got excited about applying the principle to cosmetic application. Quite a number of experiments were made with nail enamel, and one large perfume company spent a good deal of money trying to make a suitable applicator for a body cologne, but nothing seemed to come of all this until Bristol-Myers hit the market with their roll-on deodorant, which, of course, was a fantastic success.

We have not seen the roll-on lipstick, and, like most everyone else in the trade, we are inclined to cross our fingers as to its virtue lipstick in application. However, things move pretty swiftly in this trade and certainly the next six months will show whether this is a gimmick or a home run.

The booming market for men's grooming aids seems to add a new member to the manufacturer's roster at least once a month.

In addition to the general over-all expansion in product sales and in the number of competing manufacturers, there also seems to be an expansion in the scope and variety of products included in the general classification of men's toiletries or cosmetics.

For instance, it has been reported that Mennen next year will introduce 16 new products in this division.

The cost of keeping a salesman on the road in an automobile has reached an all-time high.

According to one company specializing in this sort of thing, namely, Wheels, Inc., of Chicago—an automobile leasing company drug and cosmetic industry salesmen driving their own cars on company business reached a national average of 08.87 cents per mile. The national average for all industries is 08.91 cents. In 1957 the national average was 07.72 cents.

Perfumers, who are very competent judges of alcohol quality, at least from the viewpoint of perfuming, must have been highly interested in the rush of advertising competition by the big gin distillers to register as the makers of a very dry gin. To date, three of the distillers have registered a claim for 100 per cent dry.

But what must be interesting to the perfumer is big headlines such as "Exclusive Dry Zone Process Removes All Traces of 'Sweetness' and of 'Perfume'."

According to one distiller, "We distill our dry gin in a new way we developed. In fact, our gin is refined no fewer than seven separate times. During every one of the seven refining steps, the sweet 'head' flavors rise to the top of the distillation columns and are discarded. At the same time, heavy, perfume-y 'tails' sink to the bottom and are thrown out."

Of course, after all this is completed, flavors are added. The alcohol, before the flavors, sounds like ideal perfume alcohol.

Everybody in marketing knows that the potent word 'convenience' has a lot to do with success all along the line in the marketing chain, but very few have analyzed its full force and meaning, or the multiple areas in which it occurs as a factor of essential importance.

There was a time when consumers might have walked a mile to get a particular product, but certainly that time has passed. In this era of mass marketing, convenience has become a provocatively challenging quality in distribution.

The way convenience enters into the marketing plan was recently shown in a speech by Charles G. Mortimer, president of the General Foods Corp. Although it has been widely quoted in advertising and business magazines, many of our readers may have missed it, and, since we consider his analysis of convenience in marketing so important, we are abstracting it here.

According to Mr. Mortimer, there are at least ten forms of convenience that must be considered in marketing. Each of these forms will have varying importance in different industries. Nevertheless, according to Mr. Mortimer, there is "a tidal wave of craving for convenience that is sweeping over America. Today convenience is the success factor of just about every type of product and service that is showing steady growth."

The first of the ten is *the convenience of form.* In the food field, for instance, a consumer is offered a wide choice and variety of foods in fresh, frozen, canned, powdered, flaked, solid, cake, bar, paste,

cream, or liquid form. Coffee, for example, must now be available in regular, instant, and two decaffeinated forms.

The drug industry must be equally creative in terms of convenience of form. Many drugs and toilet preparations must be available to the consumer in liquid, paste, syrup, powder, or pill form, or as an inhalant.

We suppose that the recent excitement about aerosols in our industry has added still another form.

Convenience of quantity or unit is a second requirement of consumer satisfaction, again calling for creativeness. Products of all kinds must be offered in sizes, quantities or units that suit the needs—or the whims—of the consumer.

Storage space in the average apartment or one-floor home is limited. Consequently, no grocery product must occupy more space that its importance or frequency of use dictates. On the other hand, Mrs. Consumer may go to the other extreme and insist on products in packages of jumbo size, to save her trips to the store, or to provide economy.

Convenience of time is showing increasing importance. Mrs. Consumer must be able to buy whatever she wants at exactly the time she wants to buy it—even if some retail stores have to be kept open evenings and other odd hours to suit her convenience.

Convenience of place has brought about a revolution in shopping habits. This includes the suburban shopping center, the suburban department store, the supermarket with its ample parking facilities and a host of other innovations in retailing all directed to making their store as convenient as possible for consumer shopping.

Convenience in packaging. Depending on the character of the item, its package must be easy to find on the shelf, easy to store or easy to carry in the pocket or handbag, easy to open, and easy to use. The package must protect the contents until empty, and when it has fulfilled its function it must be easy to dispose of, or else be usable in some way.

On the negative side, packaging presents a latent competitive threat which no packer or manufacturer dares to ignore, lest some more creative competitor steal the market with a more convenient one.

Convenience of combination is a broad classification which includes matched luggage, matched sets of golf clubs, food packages with ready-mixed sauces, and so forth. There are big marketing opportunities in offering the consumer unit combinations of things that are naturally used together, at a combined price. We have only scratched the surface in this marketing area.

Convenience of automation. This is a reference to such things as automatic dishwashers, laundry equipment, and thermostatic devices for regulating room temperature. We do not, at this point, think of any application of this form in our industry.

The convenience of consumer credit needs little explanation in this nation with its many billions of dollars spent on installment credit, its Diner's Club and its pursuit of the dollar by means of every imaginative credit device. We hope this will continue to be merely a convenience and nothing more.

Convenience of selection has its full application in this trade. We know only too well that a consumer wants a wide range of forms, units, patterns, models, colors, flavors, styles, and prices. Probably the cosmetic industry is the number one example of the consumer's demand for full variety and selection.

Mr. Mortimer's last convenience is the *convenience of readiness.* This is more probably a problem of the food trade where built-in-maid-service is taken for granted. "Instant" is today's magic word in meal preparation in the home. This industry wants the convenience of readiness and quick and easy application and lack of complications, but it is certainly less important here than in the food field.

These ten conveniences undoubtedly include all of the primary creative marketing problems today. The manufacturer and the retailer who can successfully offer and apply a majority of them must certainly be in a very favorable competitive position.

Coty's new aerosol purse flacon is said to be the first package in this industry to use the new plastic that originated in Italy, but is now made in the U.S.A. —polypropylene.

Polypropylene is said to have high strength and high resistance to scratching, and to be chemically resistant to alcohol, to the aerosol propellant, and to the aromatic products used in perfume.

Another highly interesting feature of Coty's package, although definitely not new in this industry, is the fact that this beautifully designed aerosol container is merely the outer shell used to protect an untreated glass bottle. For this reason, the polypropylene outer container, in addition to its decorative value, acts as an efficient shield from splintering glass in case of an explosion from the propellant. This eliminates the protective coating on the glass bottle which has come to be so widely used.

Still another feature is the way in which the bottle is anchored in the plastic container so that it cannot be removed, hence completely safe and foolproof.

The teen-age market is a spendthrift market, according to the president of the Youth Research Foundation, who says, "On the one hand teens stick doggedly to a highly vintaged pair of jeans or shoes, which should have been discarded long ago. But then again they want the latest model in most other things.

"Teen-agers are extravagant and carefully avoid the lines in savings banks. Only one out of three is committed to savings on a long-term basis. The rest are living right up to and even beyond their incomes."

The Metropolitan Daily Newspaper Market Data, a booklet which gives complete data on metropolitan newspapers and their market, has just been published by the *Richmond Times-Dispatch.*

"Pharmony" is a new word in advertising and a new word in this trade. Pharmony represents a new point-of-sale advertising in drugstores for ethical manufacturers. It is in-store broadcasting of music and discreet commercials for ethical drugs or those so-called ethical drugs, products that are available without a prescription but traditionally have been promoted only to doctors and druggists.

The first experiment will be made in 20 drugstores in the New York metropolitan area during June, July and August. The five companies who will cooperate in this test are Lederle, Ciba, Pfizer, Upjohn, and Schering.

General Foods will soon use its well-known seal on both packages and advertisements.

This industry, in which there are many companies with a broad family line of products, have not been too enthusiastic about the use of a seal.

It seems to us that it is a pretty expensive job today to create any sort of a favorable image for a company name which could be extended to a large group of products, let alone trying to identify in the public's mind a company seal.

We wonder whether a seal is a good substitute for a company image.

Who was it that first called the house-to-house food fad salesmen "Merchants of Menace?"

We do not know the origin of this intriguing phrase, but we do notice continual reports indicating that there is a vast increase in the number of house-to-house sales people with all sorts of quack nutrition products.

This country is becoming increasingly nutrition conscious, particularly in regard to vitamins, minerals, and calories, which must certainly open the opportunity for some pretty questionable activity in house-to-house selling.

Last year the book, "Madison Avenue U.S.A.," created quite a stir in advertising and marketing circles. Even in a few months a lot of things can happen to Madison Avenue. For this reason, *Printers' Ink*, in the article, "Madison Avenue, Revisited," by Martin Mayer, author of the book, has produced some interesting observations.

For instance: "Advertising has been so successful financially because it is an effective, low-risk competitive weapon. It is the modern manner of accomplishing results which were formerly—at least in theory—secured by price-cutting. Price reductions are a shillelagh of a weapon, very dangerous to all the contestants because the costs cannot be controlled, and often ineffective because each combatant has his own shillelagh. The costs of an advertising campaign can be fixed in advance, however, and if the campaign succeeds, competitors will not find it easy to fight back."

Another quote: "When a competitor's change in advertising hurts you, you aim to hurt him back. And, usually, your weapon must resemble his. When a competitor gains sales by shouting that his beverage is heavier, it appears unwise to call out that yours is lighter."

Another quote: "Perceptions—here is the magic word which reduces the forest back to trees and points the return to reality. There are endless arguments about how advertising 'works' in particular, but one generalization blankets all controversies. Advertising works by influencing consumers' perceptions of the relation between themselves and the objects advertised.

"To influence people's perceptions in areas which are important to them is an unendingly, incredibly difficult job."

An amateur might add, then what kind of a job is it to influence people's perception in areas that are not particularly important to them?

More than two dozen films available free to public, agricultural, and medical groups, are listed in a new 12-page film catalogue published by Chas. Pfizer & Co. These 16mm. sound films are offered on loan to representatives of schools, colleges, farm audiences, medical and pharmacy groups, civic and service organizations, and parent groups. Many of the films cover subjects of general interest in the fields of science, medicine, and agriculture, while others are used for teaching purposes by doctors and medical schools.

According to a recent *American Druggist* survey, six out of ten cosmetic departments are given space up front in the store. The cosmetic department is located up front in 60.2 per cent of all drug stores; it is located in the center in 34.1 per cent of stores and relegated to the back of the store in only 5.7 per cent.

According to comments on the survey, this is unquestionably the basic reason why the drug stores have held their competitive position in cosmetics.

Something new is appearing on the retail scene. This is the soft goods supermarket which started in New England, has been spreading down the Atlantic Coast and is beginning to get into the south and middle west.

The soft goods supermarket is a glamour minus retail store with four simple consumer appeals, namely, discount prices; plenty of parking space; nighttime shopping (open till 10 P.M. six nights a week); and self-service and central checking-out point.

Most of these existing discount supermarkets are

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in apparel, but they are already pushing over into a variety of other soft goods lines. Some are even installing food departments as a secondary feature.

This means that a new type of retailer will soon be competing with the toiletries and cosmetics, which already have a vast oversupply of retailers.

The plus that these stores can lend to the industry is night-time availability for sale. The minus, a determined program of discounting.

Plastic bottles and tubes, which by definition have restricted orifices, are reported to have hit a new high production in 1958 of 440,811,000 units, an increase of a little over 8 per cent over the previous year.

Plastic bottles and tubes are finding increasing uses in other industries, such as household and chemical, but the cosmetic and the pharmaceutical industries are still the primary users.

A while ago it was said that, since its dubious beginning, cooperative advertising has been used and abused with varying degrees of success and failure by suppliers and retailers alike.

Most people, at least among the manufacturers, will say that the abuse far exceeds the benefits.

There seems to be a general trend just now to reappraise cooperative advertising. Of course, this is nothing new. Reappraisals have been going on for 20 years, but the fact is that abuses are increasing, and there are some indications that Washington is looking askance at this disproportionate way of dealing with retailers.

The pharmaceutical industry has found cooperative advertising a valuable form of advertising. In the proprietary medicine business it has given an extremely valuable flexibility, and opportunity to take advantage of seasonal and territorial variations.

In the cosmetic business it has been even more valuable, particularly for the small company getting started, and the company using franchise or selected distribution.

In fact, it has been almost essential for any cosmetic company doing a substantial volume of business with leading department stores.

Although the drug chains get a great deal of cooperative advertising from toiletries manufacturers, it is to the department store that most of the money from the cosmetic industry flows, and where most of the problems arise. In fact, one could say that the department store, because of its extremely wide trading area for a single store, is the one type of retailer that could functionally use cooperative advertising to the best advantage.

However, the people in our trade are getting fed up with a number of practices in the use of cooperative advertising.

The primary grievance is, of course, the double-billing scheme participated in by many newspapers. The variation here covers the lot. It may run from a moderate mark-up of the local rate, to a store billing for a newspaper rate that exceeds the national rate the manufacturer could buy through his national advertising agency.

Added to this are all sorts of growing charges from the advertising department, which many stores now have placed on a profit-producing operational basis.

Other grievances are the distortion and mangling of advertising copy that has been carefully prepared and carefully tested; the selection of secondary newspapers in order to help maintain the store linage there; the selection of unfavorable days for the same reason; and what might be summed up by saying the practice of the store in using the manufacturer's advertising more to fortify the store's position in some way other than as it benefits the manufacturer.

Probably worst of all is the fact that more than half of all cooperative advertising appears as "Little Orphan Annies." This means that a manufacturer who has spent money with and through a store should have the right to expect some degree of interest and cooperation, at least within the cosmetic department, during the brief period in which this cooperative advertising appears. However, in an extraordinary high percentage of cases, the advertising department places the copy and then fails to notify anyone in the store, even the department concerned.

Cooperative advertising should be an essential instrument in selling, but the multiplying abuses connived in by stores and newspapers are rapidly bringing about a situation that will either destroy a large part of this advertising or pull the whole mess out into the open in an investigation which neither the newspapers nor the stores will like.

Here is what the president of a medical society had to say recently about direct mail to doctors, to the convened members of a state pharmaceutical society: "Much of this literature is never read. The most common practice in the average doctor's office is for the secretary to separate the advertisements from the first class mail and dispose of this great pile of costly literature without the physician's ever seeing it."

Unfortunately, the meeting was not followed by a question period when someone could have asked this doctor how he kept up with the continuing new developments in his profession.

A business executive asked if he could deduct the cost of the perfume given to a client's wife. The advice was 'Yes,' if he gives it to her in a bottle, but 'No,' if he helps her dab it on. This was in a story reported in *The New York Times Magazine.*

In spite of all the excitement and hurrah about non-food sales in grocery supermarkets, the percentage of sales of non-foods have remained fixed at 05.0 per cent over the last two years. Non-food sales have not been rising any faster than the sales of food.

News in Packaging . . .

1959 National Packaging Forum

Roy W. Abling of Merck Sharp & Dohme, chairman of the Packaging Institute's 21st Annual National Packaging Forum, has announced the basic program for this November's three-day meeting at New York City's Hotel Statler.

The opening meeting will be addressed by LeRoy M. King, vice-president-marketing, Food Topics and Food Field Reporter. He is a former supermarket operator.

Of special interest to the drug and cosmetic industry, among the luncheon speakers, are William C. Stolk, president, American Can Company, who will address the opening luncheon, on projecting packaging progress, and John L. Harvey, deputy commissioner, Food and Drug Administration, Department of Health, Education, and Welfare, who will speak at the Wednesday luncheon.

Other pertinent sessions include: Monday afternoon, Research and Development, chaired by Paul B. Reuman, research supervisor, research laboratories, Continental Baking Company, with speakers on unexploited functional properties of aluminum; on the need for product evaluation for thermal, corrosion or solvent resistance, etc. in rigid versus semi-rigid containers; on developments in wrapping products; on trends in packaging research in the U.S.A.; and trends in European research and opportunities for business contacts abroad.

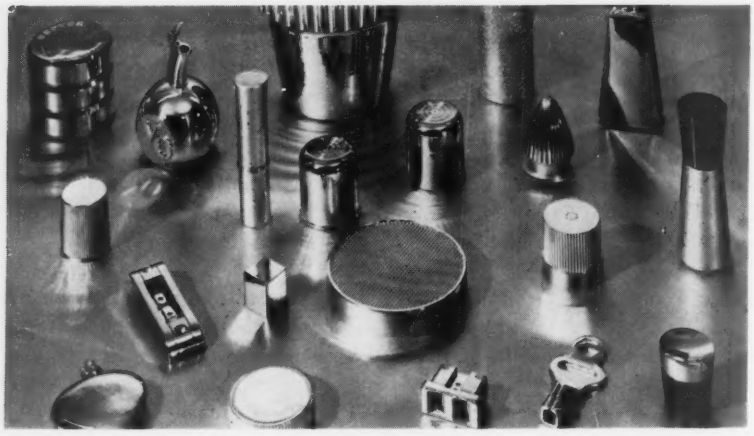
Tuesday, all day, Drug and Pharmaceutical, the morning session chaired by R. J. Hennessy, Lederle Laboratories, with speakers on design, printing and coating possibilities in glass and plastic packaging components; metal packaging developments and prospects; and design possibilities of plastics. Tuesday afternoon, chaired by O. P. Norris, Winthrop Laboratories, with speakers on glass convenience packages; metal convenience packages; paper and plastics combinations; and the use of an oxidation-reduction indicator solution to determine the oxygen barrier properties of a liquid tight package.

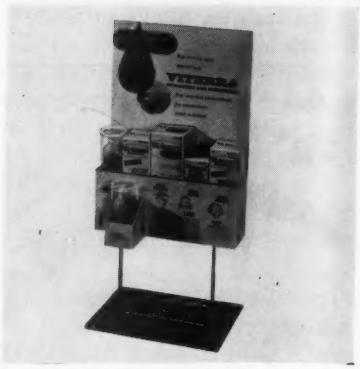
Two all-day conferences will be held Tuesday, one on production line and machinery, the other on printing, and on Wednesday morning one can attend seminars on industrial packaging, food, or closure.

A new multiple-use registration ticket is being used this year, which permits use of each day's ticket by as many as three different persons from one company, as many as nine in the three days, and includes the luncheons, as well as admission to the Packaging Machinery Manufacturers Institute exposition at the New York Coliseum on any day during its run from November 17 through 20.

Advance registration forms are available from the Packaging Institute's new office at 342 Madison Avenue, New York City 17.

Examples of parts vacuum-metallized by Eyelet Specialty Division, International Silver Company, showing the decorative and lustrous finishes that can be applied over plastics, metals or glass.





Counter display stand for J. B. Roerig's Viterra vitamin-mineral line—20 in. high, 11 in. wide, 1½ in. deep—holds 6 packages in a balcony arrangement. Individual products are described in panels on the main balcony front.

Corday's new double-strength eau de cologne in Trapeze, a fragrance introduced last year from France. Its leakproof, oval crystal bottle holds 1000 metered applications, has silvery fluted top, 2¼ oz. Cologne Concentree.

Antibiotic Spray Powder

The Surgical Products Division of American Cyanamid Company is now marketing Achromycin chlortetracycline in spray powder form for topical use. Achrosurgic Topical Spray Powder, an antibiotic spray packaged under sterile conditions in an aerosol can, is quicker and easier to apply and provides better penetration of wound surfaces than similar powders sprinkled by hand, according to the manufacturer.

Guide to Containers

The Grand-City Container Corporation, 2001 Tonnelle Ave., North Bergen, N. J., has issued a compliation of developments and trends in the merchandising of products via creative applications of corrugated and carton stocks. Titled, Ideas in Merchandising, it provides case histories, photographs, technical information, and also production innovations.

Breck Survey on Hair Preparations Issued

Results of the twelfth annual hair care survey conducted by John H. Breck, Inc., indicate that from a statistically balanced cross-section of American women, four out of five claim to have one or more hair problems—one out of three, dandruff and manageability problems, and three out of every ten, excessive dryness. Other problems include oiliness, a lack of lustre, and falling hair. Such figures indicate a continuing vast market for hair products.

Twenty-eight per cent of all women interviewed had had some type of hair coloring during the period covered by the survey, treatments being predominately of the "rinse" type.

The continued decline in the popularity of home permanents was shown in that, whereas 33 per cent of the women interviewed used one in 1957, only 27 per cent used one in 1958.

Edward J. Breck, president of the firm, said that in his opinion the greatest advances in hair preparations sales could be expected in products that afford convenience and the saving of time.

More Folding Cartons Sold

Despite a seasonal slow-down, shipments of folding cartons during July topped by 0.7 per cent those of July 1958. The total for the year is now 4 per cent ahead of the first seven months of last year in dollar volume, and almost $2,400,000 greater during the month of July than the volume during July 1958. However, new orders in July were below new orders in July 1958.

Pre-Testing of Promotions Is Essential, Muller Says

Frank Muller, merchandising manager of Bristol-Myers Products Division, Bristol-Myers Company, told the Drug Store Merchandising Clinic of the Point-of-Purchase Advertising Institute that pre-testing of promotions is an absolute essential for success in merchandising.

Mr. Muller referred to a recent comprehensive study by Horace Barry, merchandising manager for Nestle's, which showed that of about 288 national manufacturers surveyed, only 3 per cent said that they pretested their promotions and promotional ideas. Twenty per cent said they never tested them.

This seems improvident to Mr. Muller in the face of the facts that self-service drug stores are increasing rapidly, that drug stores are proliferating, and that they carry new products—40 per cent of their current business is in products that did not exist five years ago. Display materials then, are the breath of life of a merchandising program.

A Bristol-Myers survey of its sales force showed that although salesmen preferred some displays over others, they wanted a variety of displays ranging from floor stands to stickers, to suit the wide variety of drug store situations found throughout any selling district.

Mr. Muller concludes that, since well-advertised products require less time for a selling transaction, displays for nationally advertised brands should be increased and those for weak promotions or for private label brands should be decreased.

Abbott Laboratories packages which appeared in the American National Exhibition in Moscow, including the Pressure-Pak for Vi-Daylin, and table bottles designed by Raymond Lowey for Abbott's vitamins and for Sucaryl.

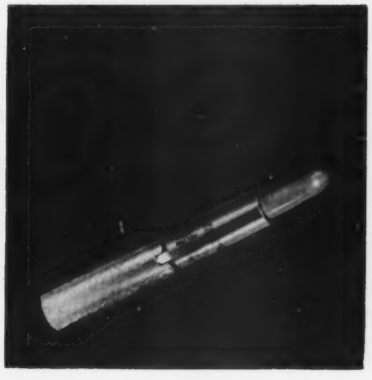
Fragonard's Zizanie Eau de Toilette in its silvery metal bottle, now an aerosol, available in two sizes, 4 ounces, $7.50, and 8 oz. at $10.00. The lemony cologne is distributed here in the United States by Carmel Myers.

Metal Use for Tubes Rises

The sharp recovery in shipments of collapsible metal tubes has shown a gain of 20 per cent over the comparable five-month total in 1958, according to the Collapsible Tube Manufacturers Council.

Lipstickles, Tussy's pomade lipsticks in limeade, cherry sundae, orange pop flavors and shades, set in metal swivel base with plastic cover matching flavor color, and holding a round mirror—all in gay counter display.

Lipline, a lipstick that functions like a lip brush, from Hazel Bishop. The Ultra-Matic top clicks off and is then clicked on to the swivel base, giving the brush length, in No Smear or Formula 77; a wide range of colors; refills.



Bufferin in a two-tablet pack for 10 cents—a foil envelop enclosed in matchbook cover, both moisture and dirt proof. The dispenser contains 50 packets, has special tab for hanging on hook, or stands on counter.

The answers to aerosol valve needs are being developed and perfected daily at Precision . . .

THIS MEANS ADDITIONAL PRODUCT SALES FOR YOU!

This new Precision spray valve, in addition to its slanted finger rest has an imprinted arrow in a second color to show the direction of flow.

A Precision stream spout for dispensing any product, regardless of viscousity, that will pour. Currently most toothpaste and syrup manufacturers, are using this practical and attractive unit.

Upside down spout, designed for toppings is far simpler to use than ordinary spouts and in addition is far easier to keep clean. Just lift and hold under the faucet.

This graceful spout has proven to be a profitable way of dispensing pharmaceuticals and cosmetics. Combined with Precisions metering valve, it dispenses a pre-determined amount with a touch.

• At Precision there is a continuing program of research and development, for each day brings new products to be packaged in aerosol containers. The success of aerosols, is based on functional design and attractive appearance for these two go hand in hand to improve dispensing and increase sales.

Perhaps your product, whether it be dispensed as a foam, a spray, a drop or a stream, should be adapted to an aerosol package. Aerosols have proven, an increase in sales because of appearance, economy and simplicity of use. Precision engineers will be most happy to talk with you.

PRECISION VALVE CORPORATION, 700 NEPPERHAN AVENUE, YONKERS, N. Y.

NEWS and VIEWS

BY TED KLEIN PUBLIC RELATIONS DIRECTOR*

Death in Man

"Death in man is accidental. It is not due to the gradual atrophy of the organs until they no longer can provide the momentum of life." So writes Dr. R. E. Tunbridge in a recent issue of the UNESCO *Courier*. He bases his statement on the fact that post-mortem examinations of individuals who lived to 100 usually revealed changes that might have caused death at any time from the age of 70.

There is evidence today to suggest that by 1980 in several highly developed democracies one-third of the voting population will be over 60 years old. The reason for the increased longevity is, of course, largely a result of improved medical care and the development of drugs which either prevent or cure disease.

The problem facing any marketer of products for the aged is an interesting one. Even though the market is continually expanding, the income for this group seems to be fixed, or even decreasing. Government statistics show that after age 54 there is a steady decline in income. And yet, this is the market for an increasing amount of pharmaceutical products.

In 1958, individuals aged 45 and over spent 66,000,000 days in hospitals. Those 65 or older accounted for 25,000,000 days. The length of hospital stay averaged over 31 days for 38 per cent of this group. This should reflect the size of the market for drugs in hospital use only.

But a closer look at the hospital population shows that many of these long-term patients are charity cases, or individuals who are partial charity cases and only able in some small way to contribute to the cost of the medical care they get.

I think that unless something is done by private individuals, the legislators will have no choice but to pass laws which will provide for medical care for individuals receiving social security benefits. Lawmakers are continual targets for pressure groups, and the aged are becoming increasingly powerful, as their number grows.

The pharmaceutical industry has an important stake in this market and therefore, I think, should advance some sort of plan for providing medical care, including the cost of drugs. If there is no way for the aging members of the population to get low-cost medical care and low-cost medicine, then the government will have to do something about it. There won't be much profit in selling to the government and government-supported hospitals or clinics.

Profit—a Dirty Word?

There seems to be considerable confusion in the pharmaceutical business on how much attention to give to telling the public about the profit a company makes selling drugs.

On the one hand, pharmaceutical PR men are instructed to be sure that stockholders know that company X is doing fine—making a sizable profit. A glance at annual reports, or an analysis of American business will show that, as an industry, we do very well when it comes to paying our stockholders dividends from our net earnings. At the same time, the PR man is instructed to make certain that the public (all those who aren't stockholders?) knows that, as co-workers in providing health services, the pharmaceutical industry is a champion working in the public interest.

There may be some doubt in the average man's mind about how a PR man can function with these two points of view. This doubt is well founded. He can't.

I have heard that students of psychology explain the confusion of many company executives when faced with this two-headed problem on the basis of unresolved guilt. In applying current concepts to the business of selling drugs to the public (via the physician) these psychologists say that the industry has developed a guilt complex. Many nuture an unconscious guilt feeling when they think that the pharmaceutical industry (and their company) prospers only as individuals become ill and need drugs.

It has been agreed that we will always be faced with public resentment over the cost of drugs, because no man likes to pay for something when he is sick. He may accept the prescription and pay the price for the antibiotic, but beneath it all he resents deeply the fact that someone, usually the druggist and the manufacturer, is making money out of his misery.

When industry leaders gather to discuss this problem, they cite unending numbers of figures to prove that today a sick man can get better quicker, through advances made possible by the pharmaceutical industry. After all, they argue, it may cost $30 for a doctor's visit and two prescriptions to treat pneumonia. But John Q will be back at work in a week, whereas, a few years ago, he would have been out for a month or more, and have spent a lot more for useless drugs.

I think that the industry is missing an important point. Ours is not a business of making sick people well. It is predominantly a business of keeping well people from being sick. To back up this statement I refer you to the industry figures on total sales of pharmaceuticals. You can see at a glance that the major part of sales is for products used as prophylactics, not therapy. Granted, we produce and sell a lot of antibiotics, but a large part of this production goes to ward off serious infection when a mild infection is present. I repeat, most of the production of drugs today goes towards keeping people well, not to making them well, once sick; or towards making well people feel better (obesity drugs, tranquilizers, vitamins, etc.).

If public relations men started using this argument on the public at large, and on physicians, a day may come when the industry will be faced with less public hostility.

Now, about that word *profit*. It is the basis of our form of government. It is a decent word, and any businessman is proud to admit it in his discussion of his company's activities. We must acknowledge this truth: We are in the pharmaceutical business to make money. Then, we must implement all-out public relations efforts with facts on how much we do to serve, how difficult it is to compete, and how proud we are that we can make a profit as we serve.

*Paul Klemtner & Company, Inc.

Patent thoughts and trends

BY THOMAS CIFELLI, JR., PATENT ATTORNEY*

Non-Nitro Musks

Musks are widely used in perfumery because of their fixative and blending properties. The natural Tonkin musk, which comes from the male deer of Tibet, is highly prized, and, as would be expected, highly expensive. It is not surprising, therefore, that chemists have long attempted to make synthetic musks to equal or surpass the natural musks in olfactory characteristics.

As a result, two main types of synthetic musks have evolved. The first is the so-called macrocyclic compound. The first one of such compounds was actually called muscone and led, incidentally, to a Nobel Prize for its inventor, Ruzicka. The macrocyclic group of musks possesses highly desirable olfactory qualities. The second group of musks that have obtained a place in perfumery are so-called nitro musks. These are usually nitration products of benzene derivatives, that is, mononuclear compounds. As may be expected, such musks do not have the odor power of macrocyclic or natural musks and, furthermore, have certain disadvantages, such as a tendency to discolor when exposed to light or alkalies.

About four years ago the chemists of Polak's Frutal Works and Givaudan announced major breakthroughs in the apparently insoluble problem of making relatively simple non-nitrated musks. The Polak product is an indane and is sold under the trademark, Phantolid. The Givaudan product is a substituted tetrahydro naphthalene and is sold under the trademark, Versalide. Some patents have appeared in this field and it is now possible to report on the present U. S. patent situation relative to these non-nitro, polycyclic musks.

Polak's Frutal Works Patents

This company has obtained the following U. S. patents to date:

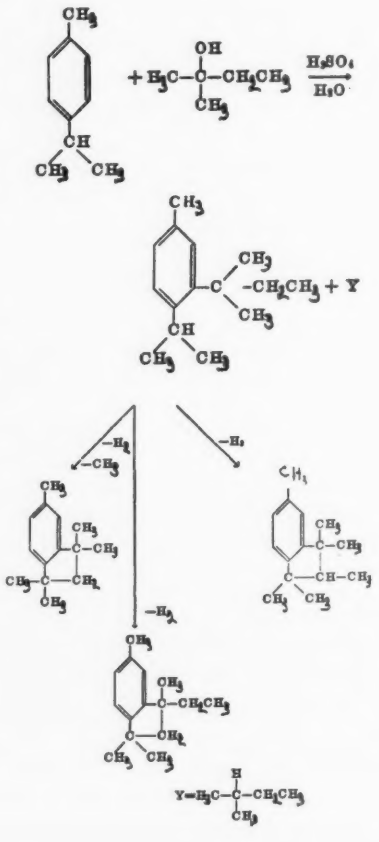
U. S. 2,752,404, issued June 26, 1956

U. S. 2,759,022, issued August 14, 1956

U. S. 2,851,501, issued September 9, 1958

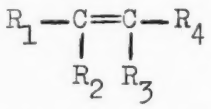
The first of these patents, U. S. 2,752,404, covers and discloses a process for making polyalkyl indanes by reacting certain secondary and tertiary alcohols or alkenes containing from 4 to 12, perferably from 4 to 9, carbon atoms, with p-cymene employing from 2 to 3 mols of p-cymene per mol of alcohol or alkene and in the presence of a liquid medium consisting of from 85 to 93 per cent sulfuric acid and from 7 to 15 per cent water at a temperature of from 20° to 50° C. The resulting indanes are acetylated to produce substances having a strong musk odor.

While the patent states that the exact mechanism of the reaction is not fully understood, it gives the mechanics of the reaction between the para-cymene and tertiary amyl alcohol as follows:



An idea of the coverage of this patent is given by claim 1, which is reproduced as follows:

"A process of producing poly alkyl indanes from paracymene, which comprises reacting para-cymene with a compound from the group consisting of secondary and tertiary saturated aliphatic alcohols and alkenes having from 4 to 12 carbon atoms, the alkenes in turn being from the group consisting of alkenes having the formula



in which R_1 and R_2 are alkyl groups containing from 1 to 9 carbon atoms, R_3 and R_4 are from the group consisting of hydrogen and alkyl groups containing from 1 to 8 carbon atoms, and alkenes which rearrange to form an alkene having said formula and said alcohols are such that upon splitting off of water they form an alkene from said group of alkenes, employing from 2 to 3 mols of paracymene per mol of said compound at a temperature within the range of −20° to 50° C. in the presence of a solution containing from 85 per cent to 93 per cent sulfuric acid and from 7 per cent to 15 per cent water."

U. S. 2,759,022. This patent, although issued after the preceding one, was actually filed about two years prior thereto.

The following example taken from the patent gives details on the preparation of what is believed to be the material marketed under the name Phantolid.

Example 1

"30 grams of anhydrous aluminum chloride suspended in 1000 grams of p-cymene are placed in the flask. While cooling the flask with ice water and agitating its contents 500 grams of tertiary amyl-chloride are slowly added. When hydrogen chloride evolution ceases the mixture is poured into cold water, the oil layer separated from the aqueous layer and the oil layer washed with water and then with dilute aqueous sodi-

*Richards and Cifelli, Newark 2, New Jersey.

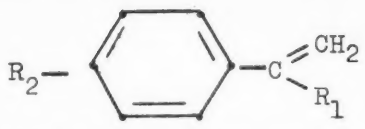
um hydroxide. The oil layer is then subjected to fractional distillation; a forerun consisting of unreacted cymene is first removed and thereafter the desired reaction product is removed. The latter distills over at about 240° to 250° C. at 760 mm. of mercury.

"This reaction product is ketonized by dissolving while agitating 100 grams of it in 200 grams of carbon disulfide, adding 80 grams of anhydrous aluminum chloride or ferric chloride and then slowly adding through a dropping funnel 45 grams of acetyl chloride while cooling. When evolution of the hydrogen chloride ceases, ice water is added and the carbon disulfide distilled off preferably with steam. The ketone is then extracted from the reaction mixture using petroleum ether or benzene for this purpose. The resultant solution is then washed with water and the solvent removed by distillation under vacuum. A mixture of ketone isomers are thus obtained as a pale yellow liquid having a boiling point of 158° −159° C. at 7 mm. of mercury and a specific gravity of 0.985 at 15° C. This liquid crystallizes upon cooling, the crystalline mass having a melting point of 25° to 46° C. By recrystallization the isomers can be separated, since they differ in their melting points. Also separation of the isomers can be effected by fractional distillation."

This patent contains claims to the novel products, claim 1 being the broadest. This claim is reproduced here:

"A photochemically stable para-cymene derivative having a musk odor and which is inert to alkali produced by reacting para-cymene with a compound from the group consisting of alkyl halides, the alkyl group of which contains from 4 to 6 carbon atoms, aliphatic alcohols containing from 4 to 6 carbon atoms and alkenes containing from 4 to 6 carbon atoms in the presence of a condensation catalyst, separating the para-cymene reaction product from the reaction mixture and acetylating the separated reaction product."

U. S. 2,851,501. This patent deals with a different process for making the polyalkyl indanes, certain styrenes being used in place of para-cymene. The styrenes should have the structural formula

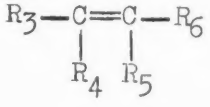


in which R_1 is either hydrogen or an alkyl group having from 1 to 3 carbon atoms and R_2 is hydrogen, an alkyl group having 1 to 3 carbon atoms or an alkoxy group having 1 to 3 carbon atoms. Where R_2 is an alkyl or alkoxy group it is on the para position of the aromatic ring. Examples of styrene compounds are styrene, paramethyl styrene, α-methyl styrene, p-α-dimethyl styrene, p-methoxy-α-methyl styrene, etc.

Claim 1, which is illustrative of the process protection obtained, is reproduced in full.

"A process of producing monomeric poly alkyl indanes from styrenes, which comprises reacting in the presence of an acid acting catalyst at a temperature within the range of from −10° C. to 90° C. which temperature is maintained throughout the reaction a styrene compound having the formula

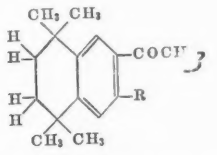
in which R_1 is from the group consisting of hydrogen and alkyl groups containing 1 to 3 carbon atoms and R_2 is from the group consisting of hydrogen, alkyl having 1 to 3 carbon atoms, and alkoxy having 1 to 3 carbon atoms, with an alkene from the group consisting of alkenes having the formula



in which R_3 and R_4 are alkyl groups containing 1 to 7 carbon atoms and R_5 and R_6 are from the group consisting of hydrogen and alkyl groups containing from 1 to 6 carbon atoms and alkenes, which upon rearrangement form alkenes having said formula, employing from 0.5 to 1.5 mols of said styrene compound per mol of said alkene, said reaction being carried out with the reactants in the liquid condition, not emulsified with water, to produce said monomeric poly alkyl indanes."

Givaudan Patent U. S. 2,897,237

This patent deals with compounds which can be represented as follows:



wherein R is a lower alkyl radical.

Example 2, which gives the details for the preparation of the product marketed as Versalide polycyclic musk is reproduced below.

Example 2

"Preparation of 7-acetyl-1,1,4,4-tetramethyl-6-ethyl-1,2,3,4-tetrahydronaphthalene

"A mixture of 93 grams of ethylbenzene and 2 grams of anhydrous ferric chloride was cooled to −5° C. and to it was added a solution of 61 grams of 2,5-dichloro-2,5-dimethylhexane in 83 grams of ethylbenzene during 30 minutes, maintaining the temperature at −5° C. and agitating continuously. The solution was quenched in water, washed to neutrality and distilled to yield, in addition to the excess of ethylbenzene, 69 grams of a colorless oil boiling at 90°/1.5 mm. Hg and having sp. gr. (25°) 0.920, n_D^{20} 1.5165, which is 1,1,4,4-tetramethyl-6 - ethyl - 1,2,3,4 - tetrahydronaphthalene.

"A mixture of 52 grams of acetyl chloride and 130 grams of the product obtained in accordance with the preceding paragraph was added during one hour to a suspension of 92 grams of aluminum chloride in 400 grams of ethylene dichloride at a temperature of 20-25° C. After quenching, washing and distilling as in Example 1 there was obtained 147 grams of a colorless oil boiling at 130°/2 mm. Hg which congealed upon standing. Upon crystallization from alcohol there was obtained 132 grams of the desired product in the form of colorless crystals of M.P. 45-46°, having a musk-like odor.

Analysis.—Found: per cent C. 83.70; per cent H, 10.00. Calc. for $C_{18}H_{26}O$: per cent C, 83.66; per cent H, 10.13.

The semi-carbazone was made and found to have a M.P. of 185°-187° C."

An idea of protection obtained is given by claim 1 which is as follows:

(*Continued on page 413*)

Looking for . . .

Solid Gelling Agent

for soap based shampoos. Pearls and thickens Miranol Amphoterics.

Versatile Non-Irritating Emulsifier

for creams and lotions

Thickener, Foam Stabilizer and Hair Conditioner

recommended for medicinal detergents, shampoos, bubble baths and sundry toiletries.

Non-Corrosive Emulsifier

for aerosol preparations.

Detergent Bars-Auxiliary Thickener

reduces 'bleed' of base syndets — gives soap like 'slip' with many syndets.

Thickener and Conditioner

for Sodium Bromate neutralizer (at alkaline ph's only)

All of the above are obtainable with One Product:

ROWAX 50

No irritating organic nor inorganic alkalies - No free fatty acids.

Rozilda services

Custom blending in bulk.
Technical Service.

Other Rozilda Products

Roterge C — solubilizer and flash foam — cloud point depressant

Roquest 244P — sequesterant for iron in caustic solutions. Used primarily in caustic for soap manufacturing to prevent discoloration and for KOH cuticle removers.

Complete line of amine condensates and lauryl sulfates.

ROZILDA LABORATORIES, INC.
44-18 Purves Street
Long Island City 1, New York

Please send me without cost sample of ROWAX 50 and data sheet.

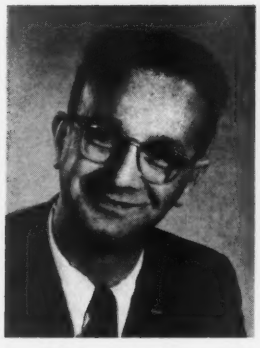
Name_____

Company_____

Address_____

City_____ Zone_____ State_____

From left to right: Edward C. Richardson, Chicago division sales manager, and Jesse H. Hallowell, Boston division sales manager, both for U. S. Industrial Chemicals Company, Division of National Distillers;



Dr. Nicholas J. Kartinos, newly named director of chemical research, Baxter Laboratories, Inc.; and Louis Amaducci, recently appointed vice-president of Norda Essential Oil and Chemical Company, Inc.

NEWS...

Appointments and Promotions

Edward C. Richardson has been appointed Chicago division sales manager for **U. S. Industrial Chemicals Company, Division of National Distillers and Chemical Corp.,** replacing George H. Stanton, who is now director of field sales. Mr. Richardson had been Boston division sales manager since 1950. He is succeeded by Jesse H. Hallowell in the Boston position. Mr. Hallowell was formerly a salesman in the Chicago sales division.

Dr. Robert M. Gesler, chief of the pharmacology section of **Baxter Laboratories, Inc.,** has been named director of pharmacologic research. Dr. Nicholas J. Kartinos, chief of the chemistry section since 1957, is now director of chemical research.

Norda Essential Oil and Chemical Company, Inc., has named Louis Amaducci as vice-president. For the past seven years, he has been in charge of plant operations for the company.

Harold J. Warnecke, manager of the northeast sales division of **G. D. Searle & Company** since 1944, has been named clinical research associate, to function in the East as liaison between physicians and the firm's clinical research staff. The firm has also named Raymond P. Hess director of sales training in the Chicago home office sales division. Mr. Hess had been manager of the Capitol sales division.

Andrew C. E. Peasco, midwest sales representative of **The Risdon Manufacturing Company** since 1947, has been appointed industrial sales manager, with headquarters in Naugatuck, Conn.

George Lueders & Company has added Kenneth E. Blauvelt and Charles E. Weeks to the firm's sales staff, the former for Pennsylvania and the Atlantic Seaboard, the latter for New York State and New England.

Raymond M. Burke has joined **Heyden Newport Chemical Corporation's** market development department. He was formerly associated with U. S. Borax and Chemical Corporation and General Foods Central Research Laboratory.

Fred K. Quigley, Jr., has been advanced to the position of staff manager of coating materials, Plastics Department, **The Dow Chemical Company.** Mr. Quigley had been assistant manager of Coatings Technical Service since 1956.

Mojonnier Associates Division, Kartridg-Pak Machine Company, has announced two appointments: Grant V. Hoyt, formerly with Aerosol Research Company and with Alpha Engineering, where he was in charge of the Aerosol Division, is now service manager and assistant to the general manager; and William Prena is product engineer. Mr. Prena was formerly chief engineer with Aerosol Research.

Kirby Peake has been elected administrative vice-president of **Carter Products, Inc.** Mr. Peake was formerly president of Vick Products Division, Vick Chemical Company, for 21 years, the last 12 as division president.

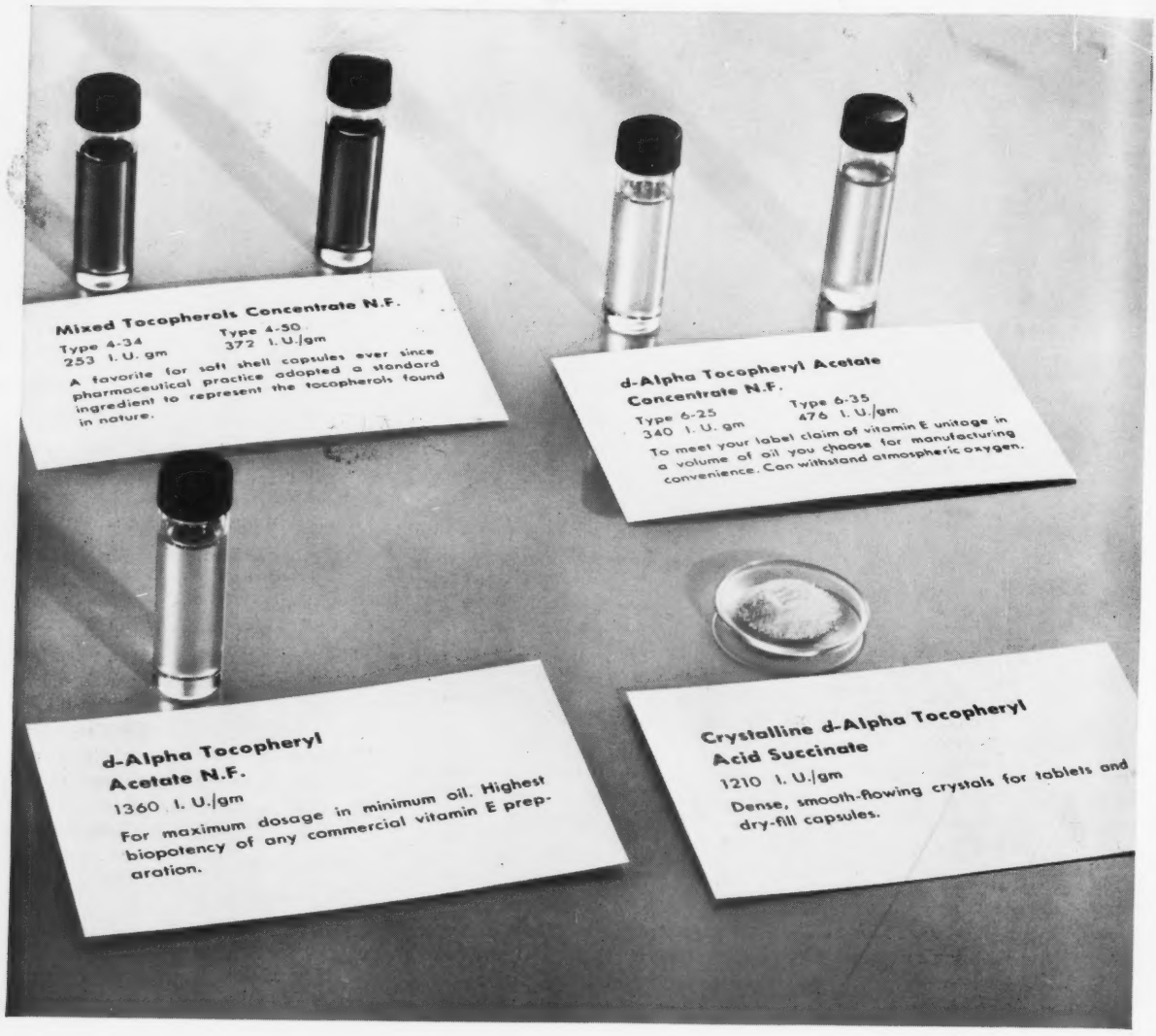
Don L. Anderson has been named assistant to the marketing manager of **Burroughs Wellcome & Company (U.S.A.) Inc.,** with principal responsibilities in new product coordination and expediting. Mr. Anderson has been a representative in the sales division of the firm since 1955.

Marion Laboratories, Inc., has appointed A. R. Haskell, Ph.D., as technical director, to expand the firm's present research and act as an advisor in the development of new products. Dr. Haskell was formerly associated with the research staff of Jensen-Salsbery Laboratories, Inc., Division of Vick Chemical Company, and before that he was a member of the faculty of the University of Florida College of Pharmacy.

Charles M. Ferri has joined **Paul A. Dunkel & Company, Inc.,** as sales and technical director. Mr. Ferri had been affiliated for 15 years with Thurston and Braidich as technical director.

Arnold J. Wasserman has been appointed to the newly created position of director of marketing for **Parfums Corday.** Mr. Wasserman was formerly marketing manager at Lightolier, Inc.

Eli Lilly and Company has opened a new sales district with Phoenix as its headquarters and Gene D. Thomas, Lilly salesman in Honolulu, as manager. John F. Raleigh has retired as manager of the Boston district. Succeeding him is William D. Cairns, formerly manager of the product addition studies department at the home office in Indianapolis. Vern H. Hakes has been promoted to director of the sales promotion division of Eli Lilly International Corporation. Mr. Hakes had been manager of the Minneapolis district until called to the home office district last December.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A favorite for soft shell capsules ever since pharmaceutical practice adopted a standard ingredient to represent the tocopherols found in nature.
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To meet your label claim of vitamin E unitage in a volume of oil you choose for manufacturing convenience. Can withstand atmospheric oxygen.
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For maximum dosage in minimum oil. Highest biopotency of any commercial vitamin E preparation.
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From left to right: Robert D. West, aerosol formulation chemist for Union Carbide Chemicals Company; R. B. Seymour, promoted to associate director of manufacturing from his former position as production manager by Aspro-Nicholas Limited, England; Mitchell E. Daniels, marketing research manager, Pitman-Moore Co.; and Dr. Bernard J. Brent, who has been appointed research director, The S. E. Massengill Co.

The **Union Carbide Chemicals Company, Division of Union Carbide Corporation,** has appointed Robert D. West as aerosol formulation chemist. Mr. West formerly formulated and tested aerosol products for Reed Research Corporation.

R. B. Seymour, production manager for **Aspro-Nicholas Limited** of Slough, Buckinghamshire, England, has been promoted to associate director, manufacturing, by the firm. Mr. Seymour, well-known in the American pharmaceutical industry, is an associate member of the American Institute of Chemical Engineers.

Mitchell E. Daniels, marketing coordinator, has been named marketing research manager by the **Pitman-Moore Company, Division of Allied Laboratories, Inc.** Harold F. Cummings has joined the firm as a vice-president. Mr. Cummings had been with Vitamerican Corporation since 1948, most recently as vice-president in charge of sales. Lloyd Alsman is now assistant to the controller, and Curtis Jordan is manager of the firm's credit department. Four new members have been added to the board of directors of Allied's subsidiary, **Campana Corporation:** John R. Jewett and Dr. Carl Bunde, vice-presidents of Pitman-Moore, and Craig Benson and Gene Pearsall, vice-presidents of Campana.

Bernard J. Brent, Ph.D., has been appointed research director by **The S. E. Massengill Company.** Dr. Brent has served for 16 years in Holland and the United States with Roche-Organon. Most recently he was responsible for all research for the Denver Chemical Manufacturing Company.

Schwarz Laboratories, Inc., has appointed Richard A. Fenderson, Jr., advertising manager. Mr. Fenderson had been assistant advertising manager with Evans Research, Inc.

The **Brockway Glass Company** has appointed William S. Borland to its field sales staff. Mr. Borland has been with Brockway since 1949, most recently in prescription ware sales.

Dr. George F. Reddish has given up his active duties as chief bacteriologist of the **Lambert-Hudnut Manufacturing Laboratories, Division of Warner-Lambert Pharmaceutical Company,** to devote full time as professor of microbiology and public health of the St. Louis College of Pharmacy and Allied Sciences. Dr. Reddish will continue as consultant to Lambert-Hudnut. Walter P. Kuenstler has been appointed director of marketing research for the consumer products division, for **Hudnut-DuBarry, Warner-Lambert Products, Standard Laboratories,** and **Parfums Ciro Divisions** of the company. Arthur Toft has been made advertising manager of the Hudnut-DuBarry Division. He was formerly product advertising manager of the Block Drug Company.

Charles E. Palmer has been promoted to merchandising manager for the **Pepsodent Division of Lever Brothers Company.** He was formerly an advertising manager with that division.

Rossiter L. Seward, Jr., has been named director of the **International Division of Endo Laboratories.** Prior to his new work, which calls for overseas expansion, Mr. Seward was director of field operations for the Far East and South African areas of Merck Sharp & Dohme International.

Executive changes and appointments at **R. D. Webb & Company, Inc.,** include: Wallace G. Brindise, formerly Chicago district manager, now general sales manager; John Yuille, formerly with the accounting firm, Arthur Anderson & Company, now Webb's comptroller; Benjamin J. Jarvis, formerly vice-president, sales, now vice-president, production at the Linden, N. J., plant; and A. Rolph Evans, formerly in charge of manufacturing, now vice-president of research and development at the Linden laboratories.

Dr. John E. Doyle and Dr. Eugene Morigi have been named assistant directors of clinical investigation for **Bristol Laboratories, Inc.** Dr. Doyle served on the faculty of the University of Buffalo School of Medicine before his appointment, and Dr. Morigi, a native of Istanbul, Turkey, had been practicing medicine at the Central Tuberculosis Clinic, Winnipeg, Canada.

Hyland Laboratories has appointed Frank J. Galloy, formerly a sales representative, to central regional sales manager.

John H. Hickling has been appointed manager-Latin American administration, a newly formed office in the **International Division, Shulton, Inc.** He had been advertising coordinator for the division. Shulton, Inc., has also announced the appointment of John C. Tobin as a product manager for the firm's women's fragrance products. He was formerly with C. J. LaRoche & Company, Inc.

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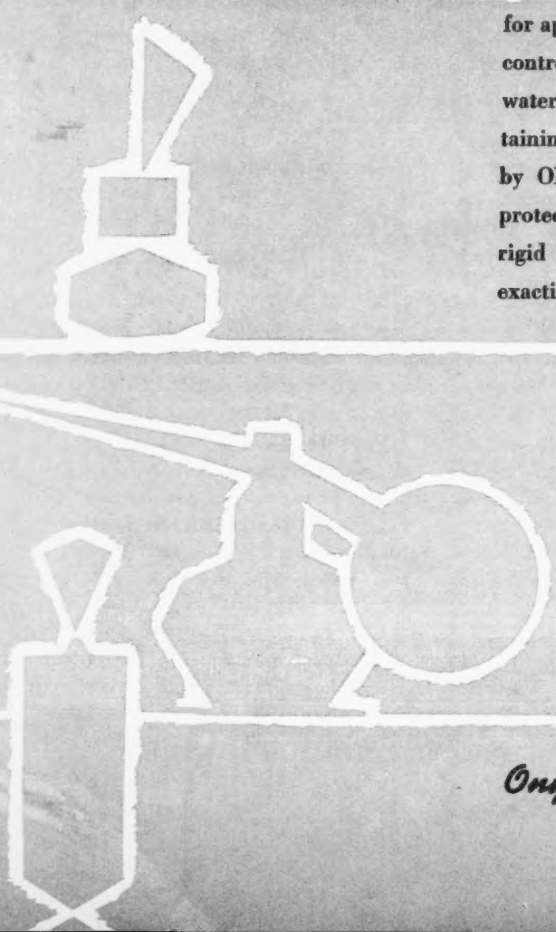
. . . the by-word in dandruff control

Improve the quality of Anti-Dandruff products with proven ISOTHAN. Now available in a super concentrated solution of 75% activity.

ISOTHAN Q-75, in concentrations of 0.1% or less (Anhydrous Basis), does not irritate normal skin or eyes. Ideally suited for applications that include rinses, hair tonics and other dandruff control products. In addition, ISOTHAN Q-75 is a light colored, water soluble liquid with a pleasant odor—a big factor in maintaining product acceptance. ISOTHAN Q-75 is compounded only by ONYX—the recognized leader in the field of anti-dandruff protection. ISOTHAN Q-75 is uniformly prepared according to rigid specifications. Close supervision is maintained through exacting quality control.



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For positive dandruff control . . . ISOTHAN Q-75 from ONYX. Additional information, samples, dermatological and toxicological studies available on request. Consult ONYX on your requirements.

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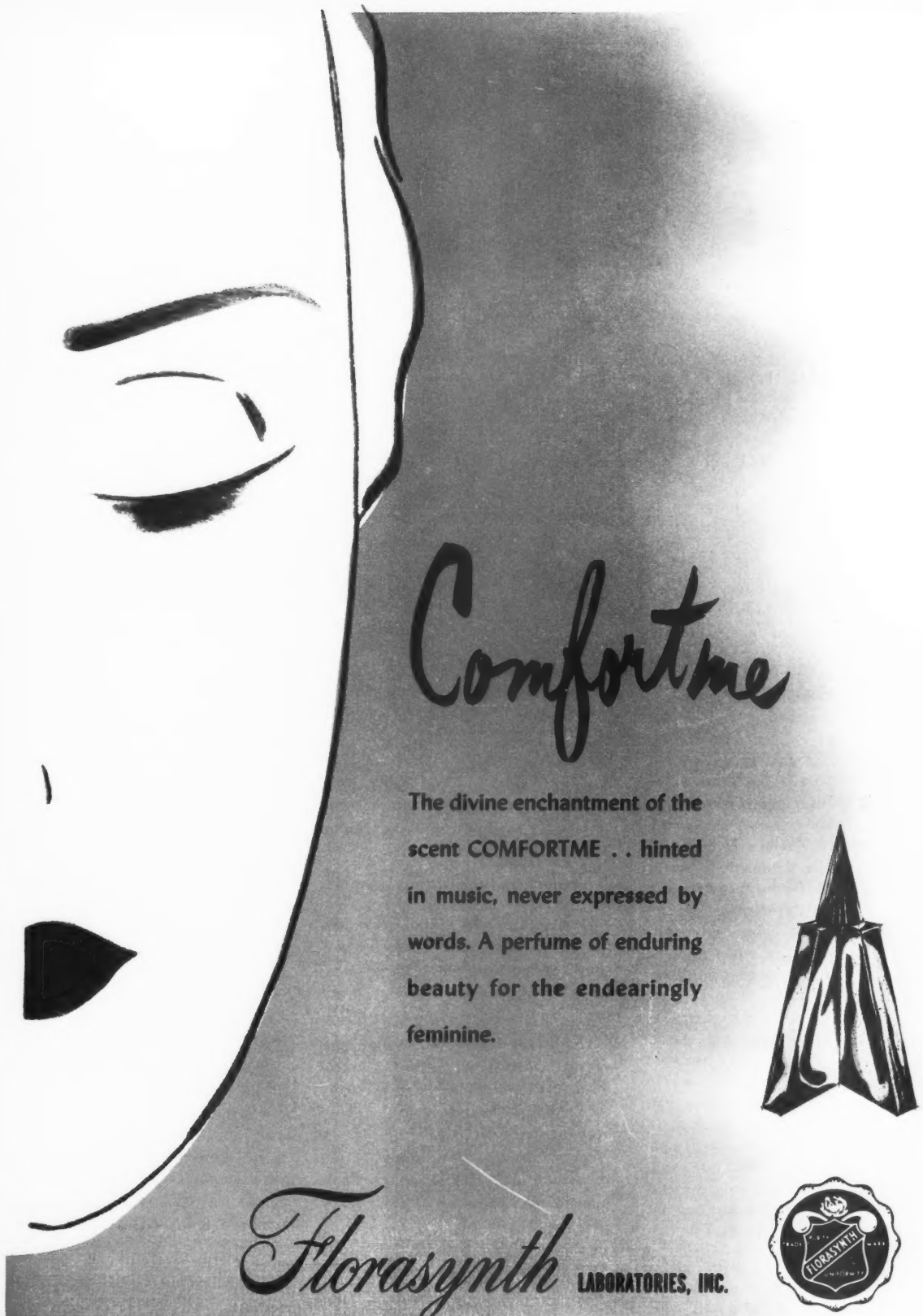
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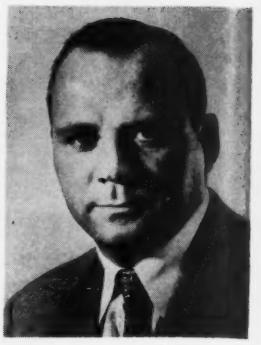


From left to right, four appointments at Chas. Pfizer & Company, Inc.: J. Philip Smith, now a vice-president and head of Pfizer Laboratories; Paul E. Weber, who has succeeded Mr. Smith as general manager of the Chemical Sales Division; George C. Mayoue, named sales manager of the Laboratories Division; and Malcolm. K. Nielsen, who has been appointed sales manager of the Chemical Sales Division.

J. Philip Smith, since 1955 general manager of the **Chemical Sales Division, Chas. Pfizer & Company, Inc.,** has been elected a vice-president and head of **Pfizer Laboratories Division.** Mr. Smith has been a director of the company since 1958. He joined Pfizer's production staff at the main plant in 1933. Paul E. Weber, formerly assistant general manager of the division, succeeds Mr. Smith as general manager. George C. Mayoue, who has been serving as assistant general manager of the Laboratories, has been appointed sales manager, and Dr. Ward J. Haas has become director of operations of the division. Dr. Haas joined Pfizer in 1954 as assistant to the director, Agricultural Research and Development Center, at Terre Haute. Malcolm K. Nielsen has been appointed sales manager of the Chemical Sales Division. Dr. Jacques M. Kelly has been named assistant to the director of analytical laboratories and quality control of the company. Dr. Kelly has spent eight years with E. R. Squibb & Sons, where his latest position was director of analytical and physical chemical research. Finally, Dr. Eric W. Martin has been appointed executive editor of Pfizer Spectrum, the firm's medical service magazine. He had been editor of the practical pharmacy edition of the Journal of the American Pharmaceutical Association, prior to which he was, from 1952 to 1956, a deputy director associated with the Physical Science Division of the Institute for Cooperative Research at the University of Pennsylvania.

Jean L. Senecal has been appointed manager of the European division of **Bristol-Myers International, Division of Bristol-Myers Company,** with headquarters at the firm's New York offices. The European division encompasses the British Isles, Continental Europe, the Iberian Peninsula, Scandanavia, and the Near East. Mr. Senecal had been associated with Procter & Gamble for 11 years before joining Bristol-Myers.

Kenneth A. Menken, assistant brand manager, has become brand manager of **Lehn and Fink Division, Lehn and Fink Products Corporation,** and Walter H. Dunnican has been named to the corporation's new position, manager of the package engineering department. Mr. Dunnican has been with Lehn and Fink since 1947, most recently as engineer in the Dorothy Gray Division.

A. G. McAdams, assistant sales manager of the **Resina Automatic Machinery Company, Inc.,** has become sales manager for the company.

Don Baxter, Inc., has appointed John G. Hainsworth director of purchases. Mr. Hainsworth joined Baxter in 1951 as a development chemist.

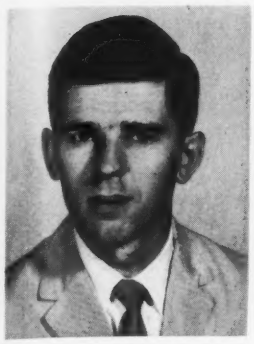
Dr. Richard Kadesch, for the past year a consultant to the chemical industry and previously research director of Emery Industries, has been appointed research director of **Nepera Chemical Company, Inc., subsidiary of Warner-Lambert Pharmaceutical Company.**

Dr. Edward C. McKeon has joined **Mead Johnson & Company** as associate medical director in the **Nutritional and Pharmaceutical Division.** Dr. McKeon has spent the past six years in the U. S. Army Medical Corps.

The **Squibb Institute for Medical Research** has announced the following appointments: Dr. Klaus Florey, formerly with the chemical development division, now director of the section of analytical and physical chemistry; Henry Roberts, from the research and development division of the National Dairy Products Corporation, now a senior research chemist in that section: Dr. Saul L. Neidleman as senior research microbiologist; Dr. John W. Ross, formerly microbiologist and biochemist with Red Start Yeast and Products Company, as senior research microbiologist; and two senior research scientists in pharmaceuticals, Dr. David Marcus in parenteral formulations, and Dr. Frank Goodhart in tablet formulations. Dr. Vincent A. Joy has been named associate director of **Squibb Clinical Research, International Division of Olin Mathieson Chemical Corporation.** Howard W. Baldock, director of advertising for Squibb, has been named director of medical relations for **E. R. Squibb & Sons.** And Fred W. Nehring, formerly clinical research associate in the St. Louis sales division, has become manager of that division, to succeed E. L. Bauer, whose new assignment is yet to be announced.

Parker McKinley Bitner, who has had 27 years of experience in the glass container manufacturing industry, has been named plant manager of the Knox, Pennsylvania, plant of **Knox Glass, Inc.**

William D. Hunt, with the **Noxzema Chemical Company** since 1955 in charge of new product development and the acquisition program, has been elected vice-president, director of product development.



From left to right: Russel J. Hahn, sales engineer, the R. T. Vanderbilt Company's specialties department; John J. Palmer and Frank J. Rubino, both vice-presidents of sales for the Peerless Tube Company; and Charles H. Zahn, national sales manager, Zenith Laboratories, Inc.

The **R. T. Vanderbilt Company** has appointed Russel J. Hahn as sales engineer for its specialties department, which produces and markets industrial chemicals. Mr. Hahn will service accounts in the middle-Atlantic states.

The **Peerless Tube Company** has announced two vice-presidents of sales, John J. Palmer and Frank J. Rubino. Mr. Palmer has been in the sales department for eight years, and Mr. Rubino has been with Peerless since 1948.

Charles H. Zahn has been appointed national sales manager for **Zenith Laboratories, Inc.** He was formerly eastern area manager for R. P. Scherer Corporation.

Ives-Cameron Company, Division of American Home Products Corporation, has appointed Michael Maiese as director of research and development, and Herbert Lowenkron as director of advertising and promotion. Mr. Maiese has been with the division since 1943, since 1946 as supervisor of research. Mr. Lowenkron has been with the firm since 1946, most recently as sales and promotion manager.

McKesson & Robbins, Inc., have announced the following executive changes: Henry H. Henley, Jr., and Dean Hildebrandt have been elected executive vice-presidents, and Charles D. Doerr and Judson C. Sutherland have been elected senior vice-presidents. Mr. Henley has served as vice-president in charge of drug merchandising, and was recently elected a director; Mr. Hildebrandt was formerly vice-president in charge of McKesson's chemical department; Mr. Doerr has been serving as vice-president in charge of personnel; and Mr. Sutherland as vice-president in charge of operations.

Chesebrough-Pond's Inc. has appointed Frank H. Orr as executive assistant to Andrew A. Lynn, domestic marketing president, and promoted Robert P. Neuffer to general sales manager, to succeed Mr. Orr.

Peter Zack, who has been serving at the New York plant, has been appointed manager, **Atlantic Division, National Can Corporation.** The firm has also appointed Gerald T. Tracy to the executive sales department, to act as liaison between sales and manufacturing on container development.

G. Edmund Heine, formerly executive vice-president of Flyndustries, Inc., packaging engineers, has joined **A. H. Wirz, Inc.,** as New York sales representative.

The **Polymer Division, Western Petrochemical Corporation,** has elected Dr. Norman G. Gaylord vice-president, research and development. Dr. Gaylord was formerly assistant director of the organic chemistry department of Interchemical Corporation.

Maurice A. Meunier, chief chemist for **Dana Perfumes Corporation** since 1942, has been named vice-president. Mr. Meunier came to this country from France in 1925. His long association with the fragrance industry includes 12 years as chief perfumer with the Colgate Company.

The board of directors of **Century Chemical Corporation** has elected a three-member executive committee: Theodore S. Hodgins, president of Century; George T. Bayley, chairman of the board of Calkin & Bayley, Inc., and Charles W. B. Wardell, Jr., vice-chairman of Deltic Corporation.

T. Nishikawa, president of the Sumimoto Chemical Company of Japan, has been named president of **Japan Upjohn Limited,** newly formed company jointly owned by Sumimoto and **The Upjohn Company;** and Norman C. Root of Upjohn International Operations, Inc., has been vice-president and general manager. It has also been announced that Dr. Bert W. Brooks has joined The Upjohn Company as director of industrial health services. Dr. Brooks has been medical director of a division of Food Manufacturers, Inc.

Donald D. Ewing has been named director of purchases for **Parke, Davis & Company,** following the retirement of Edward E. Middleton. Mr. Ewing joined the firm in 1934, and has served as assistant to the director of purchases since 1957.

Frank M. Getman, president of **Wm. S. Merrell Company, Division of the Vick Chemical Company,** has been elected vice-president of the parent firm. Vick has also announced that R. D. Waters is now president and general manager of **Vick Products Division.** He is replaced by Hermon High, as president of **Hess & Clark,** veterinary drug subsidiary. Mr. High, with Vick since 1929, has been a director of Vick since 1943 and senior vice-president since 1957.

Paul L. Hoffman has joined the pigment sales staff of **New Jersey Zinc Company,** to cover metropolitan Philadelphia, and Lloyd R. Bray has become a technical service representative with headquarters in New York City. Both have been in the firm's research department.

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Aerosol perfumes and colognes

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Superior skill, artistry, creative imagination, knowledge of consumer preferences...these are the foundations on which a successful perfume or cologne is built. But...an aerosol fragrance requires even more.

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Benjamin Cowley, president of Cowley Pharmaceuticals, has become sales manager and member of the board of directors of **Dinicol Capsules, Inc.,** a new corporation manufacturing, packaging and doing research in soft elastic capsules. Philip M. Nigro is president and Michael Di Perro is engineer for the new firm.

Sidney Fread has been appointed vice-president and treasurer of **Revlon, Inc.** He had been vice-president of finance with Joseph E. Seagram & Sons.

The **Waverly Chemical Company** has appointed Dr. Albert H. Cooper director of research and development. Dr. Cooper had been manager of the engineering research and development department of Davison Chemical Company.

Albert Findlay, with the sales administrative staff of the **Toni Company** since 1954, most recently as sales manager, has become sales administrator. James A. Torrens has been named national field sales manager. With Toni since 1946, Mr. Torrens has served in sales, price control and the Farm Service Division, General Mills.

John V. Grace, a former assistant sales manager of **Prince Matchabelli, Inc.,** has been appointed eastern regional manager.

Jerald W. Ralston, formerly with Clairol, Inc., has joined **5 Day Laboratories** as eastern regional sales manager, and Robert D. Croy, previously with Lever Brothers, has joined the firm as regional sales manager with headquarters in Cleveland.

L. E. Gaines, Jr., has been appointed sales manager of the Cincinnati district for the **Plax Corporation.** Most recently he has served as assistant sales manager in the Chicago district. David L. Anderson has become assistant sales district sales branch operation for Plax in 1955 Mr. Anderson has handled a sales branch operation for Plax in Detroit.

Fritzsche Bros. Relocate

Fritzsche Brothers, Inc., has moved its Philadelphia office to 7 Wynnewood Road, Wynnewood, Penna.; telephone: TRinity 8-7030.

Reddish Now Full-Time Teacher at St. Louis

Dr. George F. Reddish has given up his active duties as chief bacteriologist of the Lambert-Hudnut Manufacturing Laboratories, St. Louis, to serve full time as professor of microbiology and public health of the St. Louis College of Pharmacy and Allied Sciences. He continues as a consultant to Lambert-Hudnut.

GEORGE F. REDDISH

Dr. Reddish served at one time as senior bacteriologist in charge of control of antiseptics and disinfectants for the U. S. Food and Drug Administration. He joined Lambert Pharmacal Company in 1929. Since 1933 he has taught part-time at the St. Louis College of Pharmacy.

In 1956 Dr. Reddish received the achievement award of the Chemical Specialties Manufacturers Association in recognition of his work as scientist, teacher and author.

L. Cook of SKF To Give Medical Lectures

Leonard Cook, director of the exploratory psychopharmacology research program at Smith Kline & French Laboratories, has been appointed a special lecturer at the Woman's Medical College of Pennsylvania for the coming year.

Dr. Cook, a graduate of Rutgers University with a Ph.D. from Yale, has been associated with the Philadelphia firm since 1951.

Eaton's Buell Named

Charles E. Buell, Detroit representative of the Eaton Laboratories Division of the Norwich Pharmacal Company, has been installed as president of the Medical Service Society of America, the nation's professional pharmaceutical detailmen's association. Mr. Buell has been with Eaton since 1955.

Dr. Leuallen To Address Industry Pharmacists

Dr. E. E. Leuallen, Dean of Columbia College of Pharmacy of the City of New York, is to address the first fall meeting of the Society of Pharmacists in Industry, at the New York Academy of Sciences, 2 East 63rd Street, New York City. His speech, "Through the Paddy Fields with a Pharmacist," deals with the paddy fields of Formosa and Thailand.

Packaging Institute Appoints R. T. Walsh

Richard T. Walsh has been appointed membership coordinator on the headquarters staff of the Packaging Institute, a new position to provide further service to the membership. A specialist in group contact work, Mr. Walsh has been with an insurance company for the past seven years, specializing in business and group insurance and related work.

Kay Colton Studying European Cosmetic Industry

Kay Colton, manager of cosmetic sales, Morningstar-Paisley, Inc., is in Europe on a month-long search for new developments in cosmetics. Her itinerary includes the Scandanavian countries, Italy, Switzerland, France, and England.

G. Keller To Chair Travelers Fund Drive

Gert Keller of Schimmel & Company, Inc., is chairman of the Essential Oils & Extracts Division of the Travelers Aid Society of New York's 54th annual fund drive.

Left to right: George Klinger, managing editor, Drug Topics; Tom Lee, display consultant, Tom Lee, Ltd.; and Frazer V. Sinclair, publisher, Beauty Fashion, selecting winners of Old Spice Father's Day Display Contest, by Shulton, Inc.

Tyrothricin cures antibiotic headaches

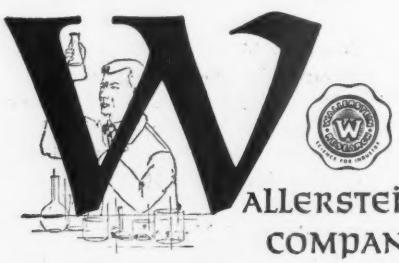
Have you run into problems of drug resistance, variable strength, and expiration dating in upgrading your products with antibiotics? Wallerstein tyrothricin can make these headaches disappear.

No Red Tape in Sales—No Red Tempers in Production

First, Wallerstein tyrothricin has never caused the development of resistant bacterial strains in animals or man. *Second,* Wallerstein adheres to rigid specs—your production and QC operations will benefit from this uniformity. *Third,* the stability and compatibility of tyrothricin exempt it from dating requirements and simplify inventory procedures. *All this adds up to a potent topical antibiotic that gives you a maximum of effect with minimum trouble.*

Cut Development Time and Costs

Whether you want to improve an existing product or engineer a new one, Wallerstein's 20 years of antibiotics research can help reduce your own development effort. Contact Gerry Gray for price schedules and *full technical information on your problems.*



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Wallerstein Manufactures Antibiotics and Enzymes for the Pharmaceutical and Cosmetic Industries

Dr. Osterberg of Abbott Laboratories Retires

Dr. Albert E. Osterberg, a well-known specialist in the field of biochemistry, has retired as a member of the clinical investigation staff of Abbott Laboratories, where he has been since 1946. He plans to spend the next few years in cancer research at the National Cancer Institute, meanwhile continuing as a consultant for Abbott.

Dr. Osterberg began his career at the Mayo Foundation in 1917, and from 1930 until joining Abbott he served as head of the section of clinical biochemistry there.

Abbott has also announced the resignation of two veteran professional service representatives, C. M. "Mort" Hotchkiss, after 32 years with the company, and George W. Borders, after 26 years of service.

Woman Receives SKF Karr Fellowship

Eleanore H. Peitisch, a literature scientist at Smith Kline & French Laboratories, is the first woman to receive the company's Walter G. Karr Fellowship for post-graduate study. Miss Peitisch will enter the University of Pennsylvania this Fall as a candidate for the doctorate in biochemistry. The grant covers full tuition and living expenses.

Larger Quarters for Century

The Century Chemical Corporation is now occupying new and larger offices in Suite 2306 of the Lincoln Building, 60 East 42nd Street, New York City 17; telephone OXford 7-4554.

Louis Schmuck Awarded Giuliana Brambilla

Louis Schmuck, secretary general of the French Society of Cosmetology, has been awarded the International Prize of Esthetics and Cosmetology, "Giuliana Brambilla," which was instituted by the firms of Laserson and Sabetay of La Garenne-Colombes, for creative but disinterested activity on the part of cosmetologists and estheticians.

Mr. Schmuck this year completed his fortieth year of uninterrupted service and devotion to modern cosmetology. For ten years as secretary general of the French Society of Cosmetology, he has contributed strongly to international collaboration among cosmetologists.

Emery To Expand

A $6,000,000 plant expansion project has been announced by Emery Industries, Inc.

New construction at the Cincinnati plant will increase several fold the present capacity for production of azeliac and pelargonic acids from oleic acid by ozone oxidation. Further construction will increase esterification capacity for Emery's line of Plastolein Plasticizers and Emolin diesters.

Hazel Bishop Consolidates

Hazel Bishop, Inc., has consolidated all activities in a newly constructed building in Lodi, New Jersey. The executive offices remain at the company's 445 Park Avenue address. The new single-story structure covers a city block.

J. David London receiving a sterling silver service for eight and testimonial scroll, for 25 years of service with Parfums Corday, from Benson Storfer, president (left), and Herbert Storfer, executive vice-president. The award dinner was held at the Chez Lucie Restaurant, New York City.

At the groundbreaking for the new plant in Whitemarsh Township, Penna., for McNeil Laboratories, Inc., (l. to r.): Robert L. McNeil, Jr., board chairman; Geoffrey S. Smith, Jr., chairman, board of supervisors, the Township; Wm. R. Davlin, Penna. secretary of commerce; Senator High Scott (Rep., Penna.), guest speaker.

Firmenich Moves West Coast Offices

The West Coast offices of Firmenich and Company, under the direction of Clive N. Ross, have been moved to 1416 Crestview Court, Los Angeles 24, Calif. The new telephone is Crestview 5-7469.

International Flavors Headquarters Consolidated

International Flavors & Fragrances, Inc., has consolidated its domestic headquarters for ALVA and P&S flavors at its Elizabeth, New Jersey location. Flavor manufacturing operations will continue at Teterboro and Union Beach, N. J., as well as at Elizabeth.

The company, formed six months ago through the merger of van Ameringen-Haebler of New York and Polak & Schwarz of the Netherlands, has also announced a new and distinctive label for its flavors materials. Label designations and numbers for both ALVA and P&S flavors will continue unchanged.

WARF Establishes Information Office

A new Information Office has been established for the Wisconsin Alumni Research Foundation, Madison, Wisconsin, with Joe Abrams as director. The Information Office is a part of WARF's Licensing Division, and will serve to keep the industry and the public informed concerning the Foundation's development and licensing activities, as well as to maintain an educational program to support the various inventions administered by WARF.

DOW | **CHEMICAL NEWS . . .** *Chemical smorgasbord for processors*

One of the big extras a chemical producer can offer a chemical processor is variety. A wide variety of chemicals gives the processor an opportunity to combine his raw-material needs in one order. And a wide variety of molecular weights, viscosities, and physical forms within each product line can have an important effect on the processor's ease of handling, storage, processing methods—even the quality of his finished product. News of chemicals for the drug and cosmetic industry—each in the Dow tradition of complete coverage within each product family—are described on these pages.

You may wish to check certain items in this advertisement and forward to those concerned in your company.

Route to:

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POLYETHYLENE GLYCOLS— "SILENT PARTNERS" FOR BEAUTY AND HEALTH

Some chemicals completely dominate a formulation—even in minute quantities. Others merely give a subtle hint of their identity. And some are "silent partners"—their contribution to a formulation is important, but their presence is not apparent. Such chemical ingredients are the polyethylene glycols. Available in twelve different molecular weights—the broadest range commercially available—Dow's P.E.G.'s are unsung heroes of the drug and cosmetic industry.

Wide-awake drug and cosmetic producers would be wise to take an appraising look at the advantages of Dow's polyethylene glycol family. Blandness, water solubility, compatibility, low toxicity are their qualifications as carriers or bases in drug and cosmetic products.

In the drug industry, polyethylene glycols have challenged the traditional grease-type anhydrous ointment bases; the bases for lotions and suppositories; the ingredients for tablet coating . . . and they are taking an increasingly broad share of the market for water-soluble ointment bases which might serve as carriers for antiseptics, penicillin, sulfa drugs, peroxides, and other medicaments.

Until the advantages of P.E.G.'s were popularized, grease-type bases were the only vehicles for substances which deteriorate in the presence of moisture. But the newcomers not only preserve the activity of medicaments, which deteriorate in the presence of moisture, they also release the medicament more quickly and efficiently.

In lotions, the polyethylene glycols replace glycerine where a milder humectant action is desired. Suppositories, too, benefit from P.E.G.'s wide range of melting points and water solubility. The high-molecular-weight polyethylene glycols give suppositories greater shelf stability under high-temperature storage conditions.

As a tablet coating, polyglycols require a much shorter coating time than sugar. And they have a better appearance, a more durable surface, and are easier to emboss than other coatings.

Cosmetic manufacturers, too, are jumping aboard the polyethylene glycol bandwagon. In their neutral, odorless, non-irritating, water-soluble way, the polyglycols make ideal silent partners as bases for glamor creams, jellies, and lotions. The polyethylene glycols offer a wide range of compatibilities and moderate hygroscopicity.

What's more, they do not decompose, and seldom react with other ingredients in the cosmetic. The preparations made with polyethylene glycols show excellent softening, conditioning, and skin-smoothing characteristics, and are free of undesirable moisture or a tacky feeling on the skin.

All the latest news and information on polyethylene glycols is contained in a new brochure offered by Dow. Write for your copy. And it almost goes without saying, that Dow invites any inquiries you may have concerning the right polyglycol for your product.

METHOCEL:

Right on the push-button

Made-to-order for smoother, creamier aerosol packaging, Methocel® synthetic gums—another group of Dow products with a big family tree—act as superior emulsion stabilizers and thickening agents, with many unique advantages over other gums: uniformity of properties, closer control of purity, unlimited availability in a wide range of viscosities, with built-in properties tailored to suit the requirements of the cosmetic and pharmaceutical industries.

Cosmetic manufacturers find Methocel, in the HG-type viscosities, ideal for use as binding, thickening, dispersing, and emulsion-stabilizing agents, and for their water-retention properties. In the Methocel family, pharmaceutical manufacturers have found a release from dependence on the natural gums and gelatin. Methocel is always uniform and its wide range of viscosities simplify development and control work.

And now, several viscosities of Methocel are being produced in granular form. Methocel granules dissolve slower, permitting a smoother dispersion directly into cold water without first preparing a slurry.

For smoother sailing in the drug and cosmetic races, send for the Methocel handbook, or report your problem to Dow Technical Service.

AROMATICS:

Wood notes in fragrance

Dow's variety of raw-material combinations available to the cosmetic perfumer are boundless. Take C·64®, for example. A synthetic aromatic chemical, it has a powerful aroma, spicy and earthy in character, and is compatible and soluble with all aromatics and solvents normally encountered in the cosmetic field.

C·64 is well-suited to any aroma where wood notes and woody effects are desired. It will accent the character of certain spice notes such as clove bud, cinnamon, nutmeg. It adds a spicy effect to the "cool" florals such as hydroxycitronellal, cyclamen aldehyde, and Lavamenthe®. It modifies the lavender-Fougere types as well as the "continental" cologne varieties. And C·64 can give long-lasting and intense effects to an oriental aroma. C·64 is only one of many aromatics which Dow has available to solve your odor problems.

★ ★ ★ ★

For further information on these products and other Dow chemicals, write THE DOW CHEMICAL COMPANY, Midland, Michigan, Chemicals Merchandising Department 921AW9.

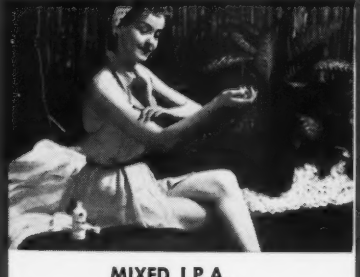
4 more—CHEMICAL FAMILY MEMBERS

CHLOROTHENE®

High quality payoff for vapor pressure depressants. Chlorothene is going great with aerosol packagers, doing the job for less money, providing higher solvency for active ingredients.

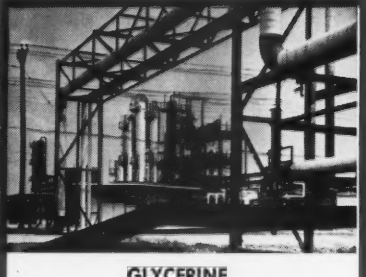
DOWANOL® DPM

Keep cosmetic and drug products clear and bright in spite of all temperature changes. Serves as a perfume fixative, lotion coupling agent, solvent in nail polish lacquers.



MIXED I.P.A.

Cosmetic emulsifier. Dow's mixed isopropanolamine offers protection against irritation; good color stability; even texture and consistency for creams; withstands temperature changes.



GLYCERINE

Old standby, Dow's synthetic glycerine has higher glycerol content, plus greater purity and clarity. What's more, it's at your fingertips—in abundant quantities throughout the country.

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Chelating Agents • Methylcellulose
Amino Acids • Fine Chemicals
Pharmaceutical and Medicinal Intermediates

THE DOW CHEMICAL COMPANY

Midland, Michigan

DOW

New Western Agency For Risdon Division

The Smith Sales Company, a manufacturer's representative and development engineering firm with headquarters in Los Angeles, Calif., has been appointed western sales agency for the Aerosol, Cosmetic and Metal Goods Divisions of the Risdon Manufacturing Company, to head sales and service in California, Arizona, and Nevada.

Reed & Carnrick Moves

Reed & Carnrick has moved into a new building at 30 Boright Avenue, Kenilworth, New Jersey, just off U. S. Highway 22. The building houses the organic, bacteriologic, pharmacological, and analytical research laboratories, as well as production, packaging, storage and shipping facilities.

Anchor Hocking Opens California Plant

The Anchor Hocking Glass Corporation has put into operation a new glass container manufacturing plant, at San Leandro, California. The plant, fully equipped for automated glass manufacturing, is on a 23-acre tract at 1940 West Avenue.

Maltbie Opens Depot

Maltbie Laboratories Division, Wallace & Tiernan, Inc., has opened a depot in Orlando, Florida, to serve the southeastern States. It is under the supervision of Adolph Kurth.

Our August Cover

By error, we attributed our August cover, which was created by Ken Rossi, to John Rosmini.

Polymer Division for Western Petrochemical

Western Petrochemical Corporation has formed a Polymer Division, with Dr. Norman G. Gaylord as research and development vice-president.

Eyelet Specialty Moves

The Eyelet Specialty Company, International Silver Company's newest division, has completed the move of its entire U. S. manufacturing facilities to International's Factory A-J in Wallingford, Conn.

Lanolin Plus Opens New West Coast Office

Lanolin Plus, Inc., has opened a new West Coast office at 610 South Harvard Blvd., Los Angeles 5, Calif., with Walter A. Page, assistant to the vice-president in charge of sales, Western Division, in charge.

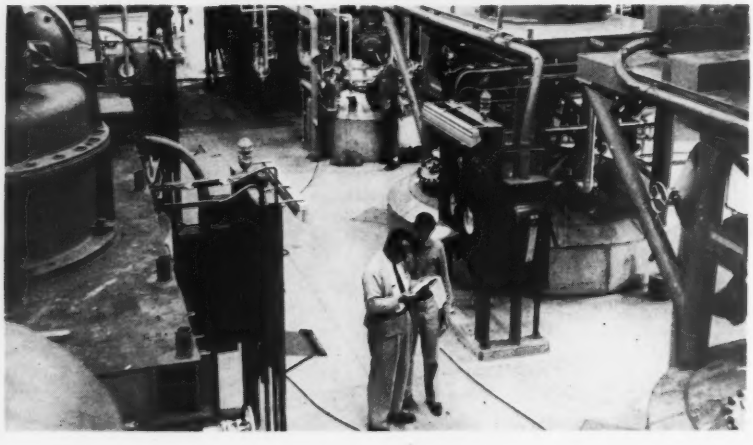
Truesdale Company Formed

P. E. Truesdale has announced the formation of the Truesdale Chemical Sales Company, for the distribution of industrial chemicals in metropolitan New York and northern New Jersey. Mr. Truesdale was formerly with McKesson & Robbins.

Oscar Beiser

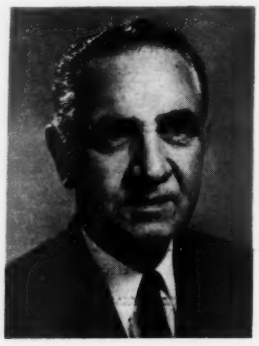
Oscar Beiser, perfumer with Armour and Company of Chicago, died August 7. In the perfume business since 1920 when he joined his brother in E. T. Beiser Company, an essential oil house, he served with Givaudan - Delawanna, Inc., from 1951 to 1958, when he joined Armour. He was a charter member of the American Society of Perfumers.

New fermenters at the Tippecanoe Laboratories of Eli Lilly and Company, part of a $2-million expansion program which includes six large fermentation tanks and four "bump" tanks. These are buried 52 feet in the ground, leaving four feet exposed, and will go into production soon.



A. Hastings Fiske

A Hastings Fiske, retired vice-president of Eli Lilly and Company, died August 25 of a heart attack.



A. HASTINGS FISKE

In his 40 years with Lilly, Mr. Fiske held many positions. Before his retirement he was a board member and served on the executive committee.

Mr. Fiske had served as assistant professor of practical pharmacy at the Philadelphia College of Pharmacy and Science before joining Lilly. He was a member of the board of trustees there, and in 1948 received an honorary Doctor of Science degree from the college.

In 1958, the American Drug Manufacturers Association honored him for his services as president in 1954-55, as vice-president for two years, and as a member of the executive committee for 11 years.

Cornelius Packard Rhoads

The director of Sloan-Kettering Institute for Cancer Research, Dr. Cornelius Packard Rhoads, died in August at his summer home in Conneticut, of a heart attack.

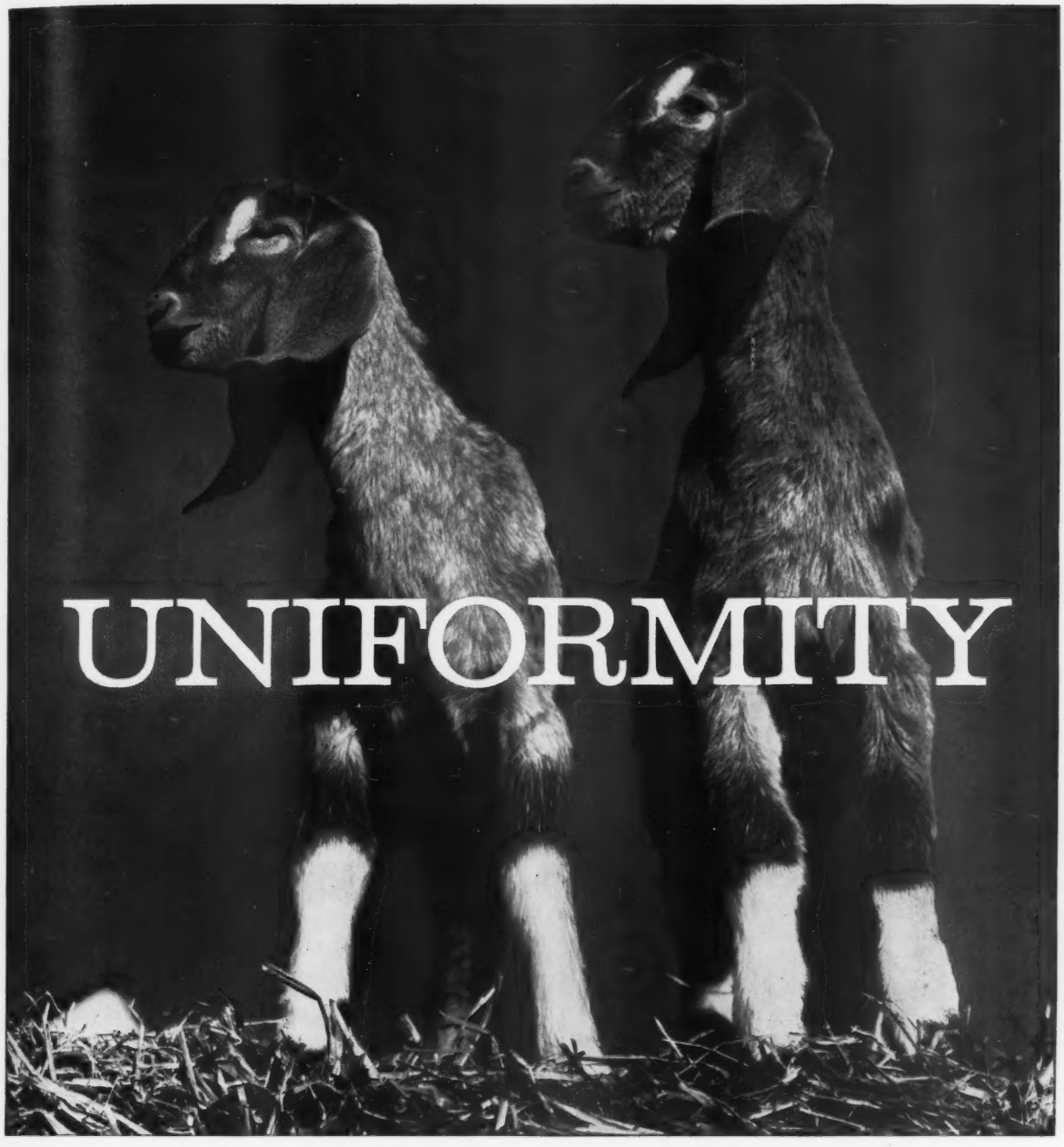
Dr. Rhoads became director of the Memorial Center for Cancer and Allied Diseases in New York City in 1940. During his stay there he revived the idea that drugs might be found to treat and even cure cancer.

After World War II, he became enthusiastic about a coordinated program for the study of cancer, and was named director of the Sloan-Kettering Institute.

William W. Gamwell

William W. Gamwell, assistant treasurer of the New Jersey Zinc Company, died on August 4 at the Roosevelt Hospital, New York City.

Mr. Gamwell had been with New Jersey Zinc since 1948.



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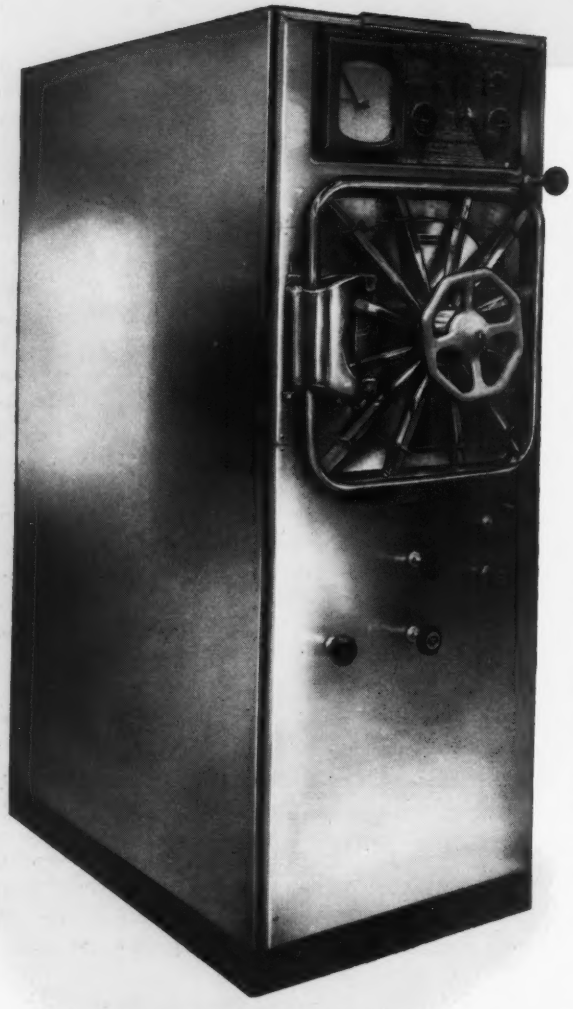

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Management Forum

BY FRANCIS CHILSON
INDUSTRIAL CONSULTANT

The Paper Flood

Once the world was flooded by a deluge of water; now it is being inundated by a deluge of paper. Letters, reports, memoranda—forms, forms, forms! The average executive's day is divided among reading, writing, and talking. He has no time for thinking. The filing department is the mortuary of dead letters and the mausoleum of wasted time. I cannot understand why executives feel it necessary to answer *all* the letters and memoranda they receive. A large share of the stuff they receive can at once be dropped into the round file. A large share of the remainder can be handled by scrawling a monosyllabic response across the top of the original document. This would save executive and secretarial time, and paper as well. But this practice will never be accepted because corporate procedure has become as bureaucratic as that of the Federal Government. Nobody is willing to commit himself unless he "covers" himself with a bit of paper.

Once I made a survey of a general office for a friend—a controller, by the way—who wanted a cold-blooded engineer's look at office procedures. The amount of duplication, useless motion, and sheer waste I found in that office, which on the surface appeared to be well organized and efficient, was shocking! As a typical example, one girl was found to have kept an elaborate set of records for nine years. She didn't know what the records were for. She didn't know who used them. It turned out that nobody used them! The head of the department didn't know the records were being kept. (Of course such a thing couldn't possibly happen in *your* office but I'll bet you a case of whiskey it does!) Records and forms have a perpetual life of their own. Once started, they grow and proliferate like cancer. Read what our friend, Parkinson (of Parkinson's Law) has to say:

"The flood of paper which now threatens to submerge the world is something peculiar to this century. The Hellenistic scribes who wrote on papyrus, the Chinese bureaucrats who exercised their penmanship on silk, and even the eighteenth-century clerks who inscribed their civilities on rag paper with a quill pen, were guiltless of any such mass dispensation of the written word as exists today.

"In a number of organizations the question is being asked whether paper work has gone too far. Some have agreed that it has. A few, a very few, have actually done something about it. In this respect, we may note a program recently undertaken by the firm of Marks & Spencer, Ltd., a British retail store organization, operating through 237 branches. Merely by deciding that the head office should trust the branch managers, and that the branch managers should trust the girls behind the counters, Marks & Spencer found that it could do away with time cards, catalogue cards, complaint reports and stock-room forms, thus eliminating 22,000,000 pieces of paper weighing 105 tons. All that they lost was a mass of statistical data of which no use, in fact, had ever been made. . . .

"If there is a moral to be drawn from this, it is that people matter more than systems. In a news account of how Marks & Spencer came to simplify its paper work, the most significant words may have escaped attention. 'It all began one Saturday afternoon,' wrote the correspondent, 'when Sir Simon Marks, chairman, visited a branch store at Reading.' Finding the girls working overtime to complete the catalogue cards, Sir Simon asked what the cards were for. No one could tell him. No one knew. No one had ever known.

"But with our praise for Marks & Spencer reorganization we must include a word of warning. To clinch their admirable reforms, the directors have set up an anti-paper committee; excellent in itself but representing, nevertheless, the thirteenth stroke of an overzealous clock. For a committee, once formed, is apt to develop a momentum and life of its own. From small beginnings it will accumulate its subcommittees, its own permanent staff. Unless Sir Simon remains eter-

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nally vigilant, his anti-paper organization will become a major department, its anti-paper directives using more paper than was ever used before."

from *The New York Times Magazine*, July 26, 1959

Industry Dispersal

During the great war, the federal government urged the dispersal of certain factories producing critical military supplies. Apart from military necessity, the idea of dispersal is good because it tends to restrict the growth of large cities. But more important than dispersal is variegation of industry. All one- or two-industry towns and cities are anachronisms. We've seen how the textile towns of New England were irreparably hurt by the removal of the mills southward. We are seeing now how the steel strike is hurting the steel-making and steel-using cities like Pittsburg, Cleveland, Detroit, Buffalo, Birmingham, Youngstown. Mechanization that reduces labor requirements radically throws limited-industry areas into a slump.

Mechanization will continue. It must accelerate if we are to continue as a world power and hold our fair share of international markets for manufactured goods. All the world is mechanizing very rapidly. Some countries have drawn abreast of us in mechanization and mass production of certain commodities, and they are in a position to use the weapon of mechanization, at least for the time being, with the additional advantage of far lower labor costs in the competition for world business. In certain areas some countries actually have surpassed us in mechanization.

There is no possible answer for us but further mechanization to a degree we do not imagine now, because costs cannot be cut in any other way. Unless a colossal depression overwhelms us, we cannot cut the cost of labor, and labor cost is fundamental to all costs. When I say "labor" I mean not only factory labor, but office or clerical labor and marketing labor as well.

This brings us back to the problems of the limited-industry areas. Ever city and town that is dependent upon only one or two industries is faced with a continuing series of depressions, perhaps permanent depressions, unless local political officials and local industrialists do everything in their power to variegate the industry within their areas. In many limited-industry areas, the local industrialists stupidly do everything in their power to prevent the encroachment of other industries. In some towns the politicians are controlled by the local industrialists, who not only try to hold labor rates down, but regard it as a healthy sign when there is a surplus of local labor.

If these idiots had any foresight, they would realize that a variety of industries simplifies union problems, provides a greater variety of skilled and semi-skilled labor and, hence, a more creative work force—a more independent work force, which is a very good thing. A variety of industries is very good insurance against serious labor disturbances. Without exception the worst strikes this country has experienced have been in the single- or limited-industry towns and cities. It is indeed a good thing that in some cities efforts are being made to variegate industry because intelligent local industrialists and politicians have experienced the disastrous results of sudden reductions in the output of specialized local industries.

The New Salesman . . .

. . . wrote his first sales report to the home office. It stunned the brass in the sales department. Obviously, the new "hope" was a blithering illiterate, for here's what he had written:

"I seen this outfit which they aint never bought a dimes worth of nothing from us and I sole them a cuple hunred thousand dollars of guds. I am now going to Chcawgo."

But before the illiterate itinerant could be given the heave ho by the sales manager, along came another letter:

"I cum her and sole them haff a millyon."

Fearful if he did, and fearful if he didn't fire the illiterate peddler, the sales manager decided to dump the problem in the lap of the president.

The following morning, the members of the ivory tower were flabbergasted to see the two letters posted on the bulletin board and this letter *from the president* tacked above:

"We ben spending two much time trying two spel instead of trying to sel. Lets wach thoes sails. I want everyboddy should read these letters from Gooch who is on the rode doing a grate job for use, and you should go out and do like he done."

Settling Strikes

Now that the steel strike is in full swing with disastrous results to the steel industry, its employees, its customers and the public, I should like to bring to your attention once again the plan I put forth several years ago in this column as a means of settling labor disputes without loss to anybody. The reaction to the plan was odd. Nobody disputed its inherent good sense. Everybody seemed afraid to give it a trial should the need arise. The personnel manager of one of the big automobile companies wrote me a caustic letter in which he said that the only way to deal with labor was to fight tooth and nail!

Inherent in the plan was the concept that a strike is as archaic in settling a labor dispute as war is in settling a political dispute.

The plan recognized certain basic facts of strikes:

(1) Management loses from three to ten times the wages lost by strikers because it cannot stop overhead expenses simply because the payroll has been stopped by the strike.

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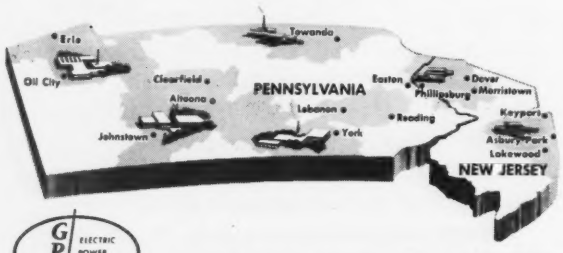
Stay right in your office—yet find the plant location you need! Simply contact GPU *Site-Service*, the one central source of plant site information for nearly half of Pennsylvania and New Jersey. You'll receive economic data covering one of the nation's most desirable growth areas with full facts about existing buildings and choice sites suitable for your needs. For this prompt, *confidential* assistance, wire, write or phone today.



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(2) Management loses the profits on business suspended by the strike.

(3) The government loses taxes on profits that would have been made had there been no strike. And local governments lose through the payment of unemployment insurance benefits while the strike is on.

(4) Customers utilizing the products of the struck manufacturer lose business and their employees lose wages because of the curtailment of routine activities. This process already has begun as a result of the steel strike. Steel users are beginning to shut down plants and lay off workers.

(5) Employees during a strike lose their wages and are forced to depend upon unemployment insurance or to get other jobs—if jobs can be obtained in the local area. Even if the strike is won by the employees and they gain substantial pay increases, months and years must elapse before they can recoup their loss of wages.

My plan suggested a means of settling strikes without loss of profits or overhead to the employer; without loss of taxes and unemployment insurance to the government; without loss of wages to the worker.

The plan would become operative after disputants in a labor disagreement had failed to reach accord even with the aid of outside mediators. The employer would be compelled by law to pay a strike bonus of five per cent of current wages to all employees involved in the strike. But there would be no interference with regular business operations. A limit would be set on strike duration and a further limit set on the time when a future strike could again be called. Negotiations would continue during the strike period with the aid of government and outside negotiators. The strike bonus would be paid to employees after the strike had been settled one way or the other.

Thus a strike could be settled without loss to employers or employees. Employees actually would gain to a limited extent win or lose. But a change in the labor law would be necessary. The minimum time for preliminary negotiations would have to be set. Employers would have to be compelled to pay the strike bonus, whether they won or not. A limit would have to be placed on negotiation time during the strike. A limit would have to be placed on the calling of another strike.

In other words, strikes as we know them would in effect be outlawed and employers and unions would be forced to settle differences by negotiation.

As a means of forcing unions to accept some such plan, I think both Federal and State laws should be changed to make it illegal for employers in an immediate strike area to provide employment for striking workers. I think also that it should be made illegal to pay unemployment insurance to strikers. I think it is immoral for employers to subsidize the strikers of other employers by giving strikers employment during strikes. The unemployment insurance law was specifically established to aid workers

who lose their jobs through economic upheavals, not to support striking workers. If the unions insist upon strikes as a means of settling disputes, let them find means of supporting strikers.

Submerged Water Pumps

The Lancaster Pump & Manufacturing Co., Inc., Lancaster, Pa., is offering a complete line of well pumps ranging in capacity from a few gallons to several hundred per minute. These pumps and motors are water-lubricated and operate submerged in wells. They are well designed and efficient, much more so, it is claimed, than conventional jet or turbine pumps. They are particularly well suited for pumping water that may contain small amounts of sand which would have a tendency to clog up the jet type of pump.

Agitator for Vacuum Dryer

The Patterson Foundry and Machine Company, East Liverpool, Ohio, has designed an agitator for use with its Conaform Vacuum Dryer called the disintegrating Conagrator, which makes possible the drying of a wide range of materials. Typical of the new range of applications when the two machines are used in combination is the preparation of materials for tableting machines, which may be blended in the Conaform and dried under vacuum at low temperature, producing a dust-free mixture.

Electro Cell

The American Air Filter Co. Inc., Louisville 8, Ky., is offering a remarkably efficient electronic air filter, available in capacities up to 240,000 cfm. Ninety-seven per cent efficiency is claimed. The design of these units is very compact, hence they are much smaller than conventional units of similar capacity.

Corrosion-Proof Pipe and Tubing

An interesting line of reinforced plastic pipe and tubing is made by Amercoat Corp., 4809 Firestone Blvd., South Gate, Calif. This firm makes all sorts of leak-proof fittings for their piping. This line is made of epoxy resin and is resistant to a broad spectrum of corrosive chemicals.

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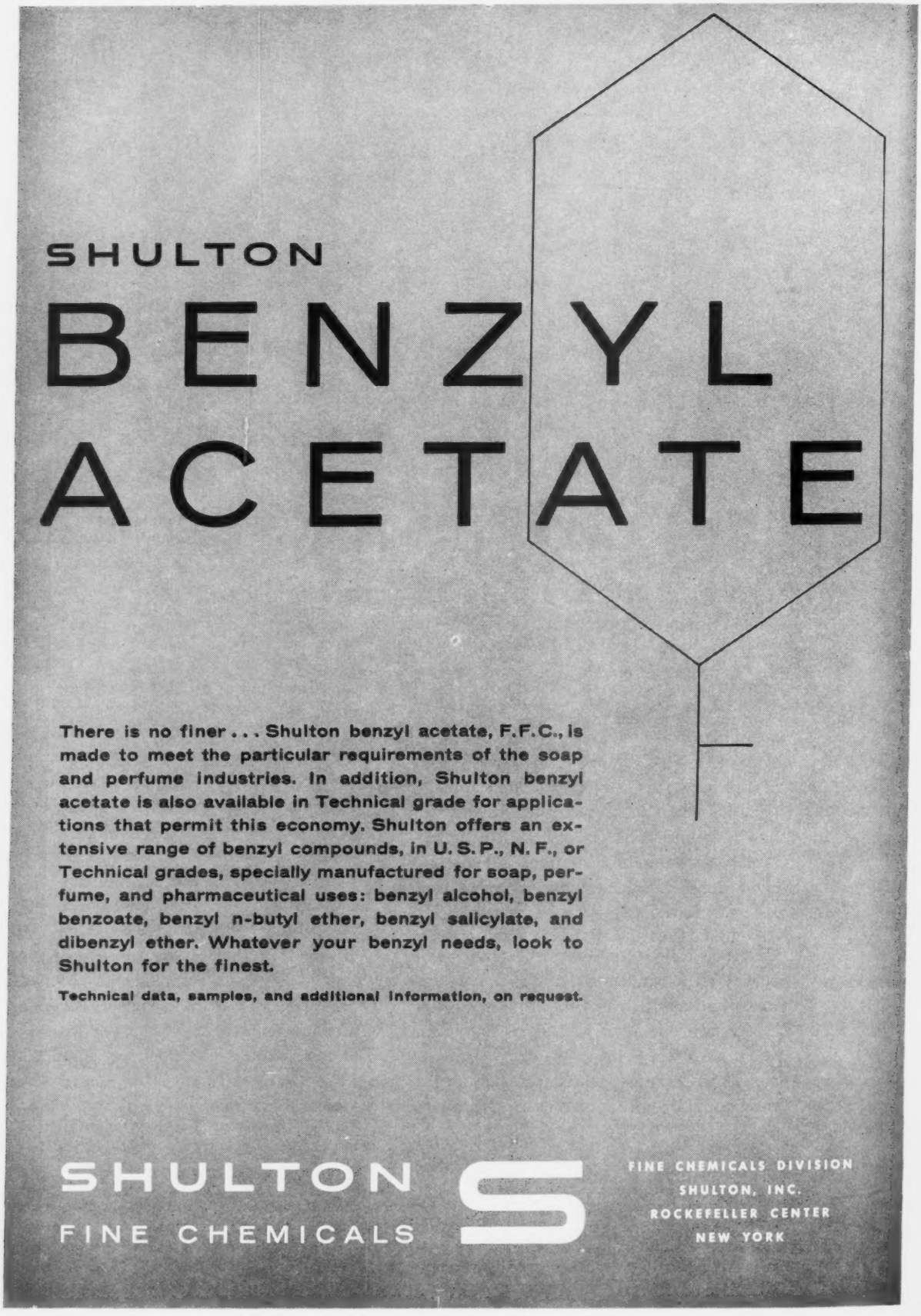
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Compounder's Corner

Hair Spray Toxicity

Bergman, Flance and Blumenthal (*New England Journal of Medicine*, 76: 471, 1958; abstracted and discussed in *Drug & Cosmetic Industry*, 82: 517, April 1958) reported two cases of suspicious shadows in the lungs, shown in X-rays, and tended to connect these shadows with the use of aerosol hair sprays. We pointed out at the time that the evidence for lung damage by aerosols was certainly not very conclusive and suggested that direct animal tests should be made. Since then, Henry J. Horn discussed the principles for evaluation of the inhalation safety of cosmetics in the *Proceedings of the Scientific Section of the T.G.A.*, No. 29, June 1958 (*Drug & Cosmetic Industry*, 83: 42, 1958). J. Calandra and J. H. Kay tested the effect of aerosol hair sprays on guinea pigs and found the animals to be unharmed (*Proceedings of the Scientific Section of the T.G.A.*, No. 30, December 1958) while J. H. Draize, A. A. Nelson, S. H. Newburger and E. A. Kelley of the Food and Drug Administration at the June meeting of the Scientific Section of the Toilet Goods Association (*Drug & Cosmetic Industry*, 84: 592, May 1959) reported that "the data from both the human and animal exposures indicate that the ordinary use of aerosol hair spray preparations of the composition and physical characteristics of those included in our studies poses no problem of safety to users."

Nevertheless, Dr. B. G. Edelston, physician-in-charge, chest clinics, Folkstone and Dover Hospitals, reports in "The Lancet" for August 15, 1959 what he considers to be "Thesaurosis Following Inhalation of Hair Spray" but which may just as readily be considered to be lung shadows of unknown origin. The case report describes a young woman who during mass radiography showed suspicious lung shadows. She had a history of cough, malaise, and loss of appetite and energy for about a year. "Questioned further, she recalled that some 12 months previously she had sprayed her hair, perhaps twice daily, with two well-known brands of fixative. She had used the spray for about six months but had then stopped, and had not used it again." Physical examination showed nothing abnormal in the chest. Chest radiography showed diffuse mottling mainly confined to the mid and lower zones of both lung fields. A variety of tests were all within normal limits and a laryngeal swab was negative for *M. tuberculosis*. At this point, without report of further clinical or laboratory work, Dr. Edelston discusses the presumed dangers of inhaling resins as suggested by Bergman, Hueper, Persson, and Altmeier. Later radiological studies of the patient showed gradual clearing of the lungs. "This case is reported in the hope that doctors will recognise the possibility that in women pulmonary shadowings of unknown aetiology may be due to inhalation of particulate matter from hair sprays." This conservative statement is followed, however, by a summary which states "In a woman chest radiographic appearances of bilateral pulmonary mottling with hilar lymphadenopathy proved to have been caused by inhalation of hair spray." If this is proof, then a lot of good scientists are wasting time doing things the hard way. The author reported no attempt to show a direct relationship between the hair spray and the lung shadows; since the cough and the other symptoms started at the time the hair spray was first used, and quite possibly before, and no X-rays were available then, the duration of the shadows is not known. No attempt seems to have been made to determine the composition of the hair sprays. No biopsy or direct examination of lung tissue was mentioned. This paper reports a suspicion and a prejudice, but not a scientific study. *Kalish*

Tablet Making

A method of manufacturing tablets has been developed by P. A. Tuerck, E. L. Walters, and E. D. Carkhuff of W. S. Merrell and reported to the August meeting of the Scientific Section of the A.Ph.A. in Cincinnati, which reduces to a minimum the normal granulating operations, amount of manufacturing time, and which enables the use of inexpensive diluents. Granulations produced by this new method have been divided into two broad classifications; low milligram potency ingredients where a major portion of the tablets may be diluent and high milligram potency ingredients where active ingredients constitute a major portion of the tablet. The method involves the use of standard coating pans in which granulations are prepared by spraying with water or starch paste and subsequent drying in the pan. The method has advantages of decreasing material costs, reducing manufacturing time and eliminating a number of processing steps, resulting in economies in labor and space.

A new rapid method of preparing granulations for compressed tablets by an air-suspension technique which eliminates the mixing, drying and grinding procedures in the conventional granulating process was presented by D. E. Wurster of the University of Wisconsin. The granulations are prepared by a particle build-up procedure in which the nuclei of the granules can be either an inert substance or a drug. Both solutions and suspensions of suitable

granulating materials in either aqueous or organic solvents can be employed.

Granules were prepared by the common wet process and by use of a screw-type extruder by P. R. Sheth and A. M. Mattocks of the University of Michigan. These were compared by means of porosity, compression curves and size distribution. Granules were compressed at various pressure levels and the tablets were compared as to friability and hardness. Extruded granules were generally found to be superior, being less porous and forming firm compacts at lower pressure. In some instances satisfactory tablets could be made from extruded granules when the usual granulation process failed.

An investigation of incorporating tablet lubricants in specific granulating agents was conducted by J. B. Appino, G. S. Bankon and H. G. DeKay, of Purdue University. The effect of the incorporated lubricants on the "fines" produced in the granulation, and on the hardness, disintegration time, and appearance of the tablets, was studied. The lubricant effectiveness was determined by measuring the relative force required to eject the tablet from the die. Experimental evidence indicated that lubricant incorporation in certain granulating agents was feasible for the formulation studied. Tablets produced with a lubricant suspension of magnesium stearate in starch paste were comparable to those produced by the conventional method of lubricant addition; but an increased percentage of lubricant was required. The tablets produced with a lubricant suspension of a stearate complex in starch paste were superior in practically all respects to those produced by adding the lubricant to the finished granulation. Tablets produced with a lubricant emulsion of liquid petrolatum in various granulating agents were inferior to those produced by the conventional method.

A modified method for lubricating tablet granulations with water soluble lubricants was presented by B. J. Munden, H. G. DeKay and G. S. Banker of Purdue University. In this process the lubricant was dissolved in certain granulating agents prior to the granulation of the tablet powder mixture. Lubricant effectiveness was determined by measuring the pneumatic pressure required to lift the bottom punch to eject the tablet. The effect on compression, tablet appearance and disintegration of the dissolved lubricant in the granulating agent was also studied. Six water soluble lubricants; Carbowaxes 4,000, 6,000, 9,000, 20,000, Myrj 52, and Brij 35 were used in this study. In the particular formulations studied, experimental results indicated that dissolving the lubricant in the granulating agent was effective. Certain lubricants actually produced better tablets when in solution in the granulating agent than when added dry as a fine powder to the granulation. An increased percentage of lubricant was usually required when the lubricant was dissolved in the granulating agent.

Antacid Studies

The preparation and properties of two new Aluminum Hydroxide-Magnesium Carbonate Dried Gels was described by S. M. Beekman of the Reheis Company to the Scientific Section of the A.Ph.A. meeting in August in Cincinnati. *In vitro* antacid evaluation tests indicate that both exhibit prompt and prolonged activity in the optimum pH range of 3.0 to 5.0. An automated gastronometer or "artificial stomach" was described. The apparatus was designed to evaluate antacids with a high degree of reproducibility.

Several new antacids were described by S. M. Beekman and C. H. Vogel of the Reheis Company. Each is a combination of aluminum hydroxide and protein in dry form. In addition to the promptness which they exhibit in raising the pH of gastric juice to the optimum level of about 4, the compositions exhibit very prolonged action in the optimum pH range of 3.0 to 5.0. All are palatable and free of chalky taste. The compositions include combinations of aluminum hydroxide with non fat milk, milk protein concentrate, gelatin, lactalbumin, egg albumin, soya protein, and casein.

Employing commercially available instruments an apparatus has been assembled by E. W. Packman, J. W. E. Harrisson and D. D. Abbott, which approaches the conditions of gastric secretion in the stomach. The acid consuming powers of the antacids when measured in terms of human gastric juice in this apparatus was up to 60 per cent greater for dihydroxy aluminum sodium carbonate and calcium carbonate and up to 33 per cent greater for sodium bicarbonate than when they are measured with 0.1 N hydrochloric acid.

Employing an alizarin impregnated test paper, the qualitative presence of aluminum on the mucosa of the rat stomach and duodenum was demonstrated after oral administration of dihydroxy aluminum sodium carbonate. In addition, the aluminum adhering to the rat stomach was quantitatively determined. A dose of 5 mgs. DASC per 150 gm. rat produced a "coating" on the stomach and duodenum which could be demonstrated for at least 60 minutes. The greater the dose administered the more prolonged was the "coating effect."

Dye Fading

The retention of color in aqueous solutions containing certified dyes (0.001 per cent) and nonionic surfactants (1.0 per cent) was measured after 14 days storage at 48.8°C. by M. W. Scott, A. J. Goudie, and A. J. Huetteman of Johnson and Johnson and reported to the August meeting of the Scientific Section of the A.Ph.A. in Cincinnati. Six dyes (FD&C Blue #2, Yellow #5, Red #1, Red #4, Green #1 and D&C Orange #3) and five commercially available surfactants (Tween 20, Brij 35, Igepal CA-710, Myrj 52 and Pluronic F-68) were included in the study. In all but four of the thirty systems examined, accelerated fading was noted over that obtained with solutions of the dye alone.

No-Smear Make-Up (Hazel Bishop) is an eye make-up line that will not smear, smudge or rub off. The line will include roll-on or cream-type mascara, swivel-stick eye shadow and eyebrow pencil-eyeliner combination.

Blue Mink Shampoo (Lawrence Pharmaceuticals) contains pure ranch mink oil and as an introductory offer is being sold for 79 cents for a 16 ounce bottle.

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Shipments of CARBIDE's triethanolamine are made in 55-gallon drums, LCL or carload lots; you can save by ordering in combination with other CARBIDE products. Ask a Technical Representative in any CARBIDE office for information on possible savings through choice of shipment's size.

Starting formulas for a variety of cosmetic products are included in the 100-page book, "Emulsions and Detergents." In addition, you'll want a copy of "Alkanolamines and Derivatives," containing information on applications and properties of CARBIDE ethanolamines. For a copy of each book, write Dept. HN, Union Carbide Chemicals Company, Division of Union Carbide Corporation, 30 East 42nd Street, New York 17, N.Y.

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Industry's Books . . .

Source Book of Industrial Solvents, Vol. III (Monohydric Alcohols), *by Ibert Mellan, Director of Research, Polychrome Corp., 276 pp., Reinhold Publishing Corp., New York, (1959), cloth,* **$10.**

The third in a series, this volume presents the physical properties, azeotropic mixtures and uses of industrial alcohols. The nomenclature includes commercial names where applicable. A historical survey describes the early production by malting and brewing and leads up to present day synthesis — Fischer-Tropsch, Isosynthesis, Oxo Process and the Oxyl Process. Methods of manufacture and newer methods of fermentation are also discussed. The book includes many significant tables and figures. Because alcohol solvents enter into every kind of industrial activity, this handy reference fills an urgent need for a convenient source of information on these substances.

Some Pharmaco-Historical Guidelines to the Literature, *published by American Institute of the History of Pharmacy, Madison, Wisc. paper,* **50c.**

This contains three bibliographic essays by: Glenn Sonnedecker—on pharmacy; J. Hampton Hoch—on pharmacognosy: and Wolfgang Schneider — on pharmaceutical chemistry.

Symposium on Nuclear Sex, *Edited for the Organizing Committee by the Secretary, D. Robertson Smith, M.D., William M. Davidson, M.D., 188 pp., Interscience Publishers, Inc., New York, (1958), cloth,* **$3.50.**

The present widespread interest in the subject of nuclear sex began with the discovery by Barr and Bertram in 1949 of a sex difference in the nuclei cells. A Symposium was held in September, 1957, at King's College Hospital Medical School and this book is a complete account of the proceedings together with a short introductory historical note by Professor Barr. Those concerned with almost any branch of biology, human or animal, will find much of interest here.

Asbestos — Its Industrial Applications, *by D. V. Rosato, Engineering Consultant, 214 pp., Illus., Reinhold Publishing Corp., New York, (1959), cloth,* **$5.75.**

This volume identifies the broad usage of asbestos in industry, and presents data on its properties and manufacturing methods. It serves as a convenient guide to various industrial branches including research and development groups, manufacturers, engineering schools, market research groups and sales management.

Radioisotopes For Industry, *by Robert S. Rochlin and Warner W. Schultz, General Electric Co., 190 pp., Reinhold Pub. Corp., New York, (1959), cloth,* **$4.75.**

There is scarcely an industry that cannot benefit from the use of radioisotopes in a great variety of ways. It is the purpose of this book to show industry exactly how it's done. A random sampling of industries would include plastics, petroleum, paper, paint, steel, mining, food, autos, electronic, chemical, drug, glass and textile, to name just a few.

Harper's Bazaar Beauty Book, *by the editors of Harper's Bazaar, 213 pp., with drawings, Appleton-Century-Crofts, Inc., New York, (1959), cloth,* **$4.50.**

Every woman has at least one acquaintance who seems to ride the years with grace, acquire admirers effortlessly and even teach her children to have a well-groomed look from cradlehood up. How does she manage to do it? What is the secret which makes her unique among her friends? The editors of America's well-known fashion magazine give you the answer, explaining just how you can build confidence and make the most of your natural assets. With the aid of this book you can learn how to look your best, to have that air of naturalness and unawareness which is the very essence of chic.

Principles and Practice of Gas Chromatography, *Edited by Robert L. Pecsok, Associate Professor of Chemistry, University of California, 225 pp., John Wiley & Sons, Inc., New York, (1959), cloth,* **$6.75.**

Gas chromatography is currently the fastest growing field in analytical chemistry. The first part of this book discusses theoretical principles underlying partition chromatography and describes the mechanism of separation when the mobile phase is an inert gas. This is followed by a more detailed description of the mobile and stationary phases. The practical details and general procedures are then described in chapters covering the effects of operational parameters, column selection and construction, sample introduction, and temperature control. General methods available for converting the experimental data into useful results are discussed in the final chapter on analytical methods.

Continuous Analysis of Chemical Process Systems, *by Sidney Siggia, Manager, Analytical Service, Olin Mathieson Chemical Corp., 381 pp., John Wiley & Sons, Inc., New York, (1959), cloth,* **$8.50.**

Details on all phases of the new analytical devices designed to attain economical, accurate, and continuous monitoring of chemical process systems are presented here. Differing from conventional lab devices, the continuous, on stream analytical instruments function automatically and directly in the processing equipment or pipeline. Recorder charts and dial readings permit a constant check of the chemical composition in process systems. Siggia also gives examples of the use of each instrument in specific applications.

Hot Organic Coatings, *by Raymond B. Seymour, President, Alcylite Plastics and Chemical Corp., 233 pp., Illus., Reinhold Publishing Corp., New York, (1959) cloth,* **$7.50.**

The constitution, applications and properties of hot organic protective coatings are concisely presented here. The book contains chapters on widely used hot organic coatings such as asphalt, coal tar pitch, petroleum waxes and cellulose derivatives. Specific information on formulations of proprietary products is included.

Synfleur perfumes are backed by more than a half-century of successful research, development and manufacture. Established in 1889, Synfleur has pioneered a large number of quality flavors and fragrances and constantly keeps abreast of new trends and discoveries to supply industrial needs. This extensive effort has resulted in a comprehensive line of perfumes especially developed for use with aerosol propellants — fragrances that rank high on consumers' preference lists. That's why Synfleur perfumes will help sell your aerosol products and keep them sold! They're yours for bigger profits.

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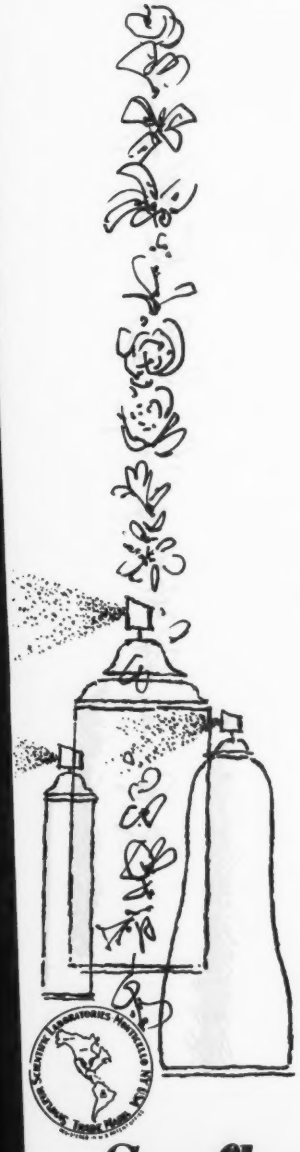

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Cedar	DH-127
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Perfumer's Shelf

Indoles

Indole and its methyl homologs (skatole; *alpha* methylindole; *alpha, beta* dimethylindole) are very valuable in perfumery. Although these substances have an unpleasant fecal odor when concentrated, in diluted form they considerably improve floral odors, making them livelier and headier.

It is interesting to note, according to Ortoli (*France et Parf.* vol. 2, No. 11, p. 19, 1959) that jasmine absolute directly extracted from the flowers contains no indole. When the flowers are treated by enfleurage, however, chemical reactions continue in the cut flower and the absolute formed contains indole. Indole is probably present in the flowers as a glycoside, which is broken down by plant enzymes. Indole is also present in the natural oils of neroli, of *celtis reticulosa,* of *robinia pseudoacacia,* etc. It must be used in only very small percentages; in excess, it not only destroys the floral quality of the perfume but also causes troublesome discoloration, ranging to red brown.

Skatole is present in the oil of *celtis reticulosa* wood and probably also in civet. In concentrated state it has a very powerful fecal odor but when diluted imparts a civet animal note; it must be used with even more care than indole.

Alpha methylindole, *alpha, beta* dimethylindole, and *beta* ethylindole are sometimes used in perfumery since they have softer notes than indole or skatole. They possess the same disadvantages, however, when used along with vanillin, heliotropine, anisaldehyde and nitro musks, or in alkaline media, when they will cause discoloration.

Thus, indole and its homologs, certainly very useful from an olfactory point of view, are difficult to use because of numerous odor and chemical incompatibilities.

Nerone

Nerone, a brand of menthenyl ketone, is being offered by Givaudan-Delawanna, Inc., as a pure synthetic aromatic chemical to impart a natural note to synthetic mixtures. The colorless to slightly yellow liquid, specific gravity 0.910 to 0.915, refractive index 1.465 to 1.475 is levorotatory and has a fresh leafy odor recalling petitgrain oil. It is very stable and will not discolor soap, is miscible in all proportions with corn oil, mineral oil, benzyl benzoate, diethyl phthalate, glycerin and dipropylene glycol, is not appreciably soluble in propylene glycol and is clearly soluble in nine parts of 70 per cent alcohol, two parts of 80 per cent alcohol or one part of 90 per cent alcohol. When tested with rats, its oral toxicity is low.

Although not a new note, Nerone being almost identical to petitgrain, it offers many possibilities for original compositions as a concentrated note free from terpene and ester components. It provides in a synthetic the odor effect of the exotic ketone portion of essential oils, especially valuable in creating the effect of natural geranium, lavender, neroli, vetiver, bergamot, lemon and petitgrain. Aldehyde C-10, isoeugenol and citrus oils are useful companion notes.

A variety of different odor effects have been realized with Nerone.

In mimosa, gardenia, violet and jasmin, a small concentration (1 to 2 per cent) gives a green petal effect not too different from the effect of a touch of neroli oil. In geranium, fougere, spice and lavender compositions, 2 per cent to 7 per cent gives natural freshness. In amber and mossy compositions, about 5 per cent intensifies and lifts the oak moss and labdanum notes and gives the perfume a velvety diffusiveness.

Various materials were combined in different proportions and several tempting odor themes were discovered. For example, a mixture of 43 per cent hydratropic aldehyde and 57 per cent Nerone gave a spicy green fragrance that suggested a pungent "aldehydic" note with a violet undertone.

Soap cakes containing 1 per cent of Nerone were prepared and left exposed to daylight and air. The fragrance in the fresh cake was strong, with an earthy herbaceous odor reminiscent of notes found in petitgrain oil. After accelerated aging and "sun exposure" tests, the cake was practically equal in odor to the unaged cake, indicating excellent stability. There were no signs of discoloration in any of the test samples. A test cake after two years of normal aging was found to be strong in odor and still retained the basic odor characteristic of Nerone.

Typical bergamot and lavender compositions for soaps and detergents containing Nerone were evaluated in soap cakes with excellent results. Nerone also fortifies petitgrain, vetiver, and geranium with excellent retention of natural odor.

The use of Nerone is recommended to the perfumer for essential oil problems concerning petitgrain, oakmoss, bergamot, neroli, patchouli, vetiver, geranium, clary sage, lavender, lemon, and orris concrete.

Second International Congress of Essential Oils

This Congress took place in Municipal Casino at Grasse in July 1959 and some of the papers given are abstracted below.

Y. R. Naves found that the essential oil of *Baccharis genistelloides* Pers. contains about 55 per cent of the acetic acid ester of monocyclic terpene alcohol $C_{10}H_{16}O$, along with 6 to 7 per cent of the free alcohol and nopinene. This alcohol is an *ortho* menthatrienol and it can be assumed to have been produced in the plant by the cyclization of a pinadienol. Its production fits in with the 'isoprene rule." Numerous derivatives have been prepared and the structure of the products has been confirmed by synthesis. This seems to be the first time that an *ortho* menthane terpene skeleton has been found in nature.

M. P. Teisseire determined the composition of fractions of French and Russian Clary Sage Oil by means classical analytical methods and vapor-liquid partition chromatography. These methods permitted the identification of *alpha* pinene, camphene, *beta* pinene, myrcene, limonene, *beta* ocimene, cineol, *para* cymene, allo-ocimene, the C7, C8, and C9 aldehydes, benzaldehyde, *n* hexanol, hexenol, octenol. Several other substances were found but could not be characterized. Extreme care must be used in interpreting chromatographic results since some products undergo transformation during chromatography.

Chemical analysis has demonstrated the presence of various hydrocarbons, alcohols, phenols, aldehydes, ketones, acids, and esters in rose oil obtained from *Rosa Damascena*. *D. Ivanoff* and collaborators have used paper chromatography and discovered a number of new constituents. The chromatographs of the 3,4-dinitrobenzoates showed the presence of methyl and nonyl alcohols; the 2,4-dinitrophenylhydrazones permitted the identification of acetaldehyde and propionic, valeric, salicylic, cinnamic, and phenacetic aldehydes. Hydroxamic acid permitted the identification of acetic and valeric acid esters.

F. LaFace identified a number of new constituents in oil of bergamot, sweet orange, bitter orange, and tangerine oils by means of column, paper, and gas chromatography and U.V. and I.R. spectroscopy. The following were identified in bergamot: geranyl, terpenyl, and neryl acetates; geraniol and nerol; C9, C10, and C12 aldehydes and probably citral; For lemon oil, the new compounds were the hydrocarbons octyllene and *p* cymene, linalol and isopimpinelline. In sweet orange oil the compounds were *alpha* and *beta* pinene and myrcene; neroli, geraniol, and linalyl acetate. In bigarade oil, the terpene fraction had the same qualitative composition as in sweet orange oil. In mandarin oil, whose composition is least well known of those studied here, were found *alpha* and *beta* pinene, camphene, *gamma* phellandrene and *p* cymene along with limonene, linalol, nerol, terpineol, the aldehydes octylic, nonylic, decylic, dodecylic, citral and citronellal, linalyl and terpenyl acetates.

E. Lederer studied the less volatile components of jasmin oil and discovered free phytol and two new aliphatic diterpenes: isophytol and geranyl-linalol. The latter is probably an important intermediate in the synthesis of phytol, di- and tricyclic diterpenes, carotenoids and of some minor components of jasmin oil.

V. Herout proved that ledol and viridiflorol are stereoisomers of globulol; their relationship and the relationship with the two aromadendrenes was established. *Alpha* and *beta* betulenols possess a secondary alcohol grouping in the caryophyllane skeleton. The structures of a group of cyclic compounds containing a 10 membered ring was also studied: germacrone, costunolide, cnicine, parthenolide. The absolute configuration of several asymmetric centers in these substances was determined.

W. Treibs reported that pinocarvyl acetate is isomerised by boric anhydride to myrtenyl acetate. Pinocarveol gives, without rearrangement, stable crystalline addition products with halogen acids and these may be reduced to pinocampheol and are transformed into campheolene aldehyde by silver acetate or organic bases.

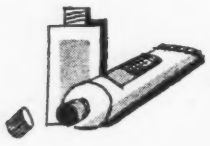
For the last 10 years, a selected variety of lemongrass has been cultivated in Italian Somaliland and this provides a remarkable essential oil. *P. Rovesti* and *G. L. Variati* studied this oil and found it to contain a very high percentage of citral with very little methylheptenone, which makes the oil especially suitable for the production of good quality citral.

Erythromycin Ester Alkyl Sulfate

While the propionyl ester of erythromycin has found wide usage in capsule form, its utilization in a flavored suspension has been prevented by its bitter taste which is quite pronounced in aqueous suspensions. It also has been observed that the capsules give somewhat lower blood levels in the non-fasting patient than when ingested on an empty stomach. The alkyl sulfate salts of propionyl and other esters of erythromycin have been found to have very low water solubility according to V. C. Stephens, J. W. Conine, and H. W. Murphy of Eli Lilly and Company and are, in most cases, completely tasteless. Therefore, they can be readily used in pleasantly flavored suspensions. Since they are salts of strong acids, they are not readily converted to soluble salts by treatment with mild acids. When exposed to gastric juice they remain undissolved and unchanged and are thus protected from inactivation in their passage through the stomach even in the presence of food. The salts can be readily prepared from the appropriate esters or by acylating erythromycin in slightly acidic solution and then isolating the desired salt by a double decomposition with a sodium alkyl sulfate.

Propionyl erythromycin ester lauryl sulfate (PELS) has been found to have very low water solubility and is readily usable in pleasantly flavored suspensions. Chronic toxicity studies in rats and dogs by R. C. Anderson, C. C. Lee, H. M. Worth and P. N. Harris have demonstrated the absence of organ or blood damage following large doses for over 3 months. Oral administration of PELS produced higher serum concentrations in rats than propionyl erythromycin. Both antibiotics are mainly absorbed from the intestine of rats and excreted in very small quantities in the bile. High concentrations of erythromycin activity were found in the lung, spleen, liver, kidney and heart after oral administration.

These papers were presented before the August meeting of the Scientific Section of the American Pharmaceutical Association in Cincinnati.



Advancing Therapy

Psicofuranine Antibiotic

A unique new antibiotic, psicofuranine, has been discovered, isolated and studied by T. E. Eble et al. (*Antibiotics and Chemother.* 9: 419, 1959). It is produced by *Streptomyces hygroscopicus* var. *decoyicus.* Antibacterial and antitumor activities are also reported by Lewis et al and Evans and Gray. Schroeder and Hoeksema have established the structure of this antibiotic to be 6-amino-9-*D*-psicofuranosyl purine. A similar compound, angustmycin C, has been reported previously to be biologically inactve, optically inactive, and to have a melting point of 198°C. In contradistinction, psicofuranine was biologically active, optically active, and melted at 212-214°C.

Psicofuraine is a white crystalline solid which melts at 212-214 C. (dec.). Analytical data and electrometric titration data are in agreement with a molecular formula of $C_{11}H_{15}N_5O_5$. Psicofuranine is very soluble in dimethylformamide, dimethylsulfoxide, and hot water. It is soluble at room temperature in the following solvents: water, 8 mg./ml.; methanol, 8 mg./ml.; ethanol, 6 mg./ml.; 1-butanol, 2 mg./ml.; and ethyl acetate, 0.23 mg./ml.

The specific rotation of psicofuranine is $[\alpha]_D^{25} = -53.7°$ (*c*, 1 per cent in dimethylsulfoxide) and $[\alpha]_D^{25} = -68°$ (*c*, 1 per cent in dimethylfomamide). Stabiilty studies indicate that psicofuranine is least stable under acid conditions, having a half-life at *p*H 2.0 and 30 C. of 18 hours. It is most stable at neutral *p*H in the temperature range 0 to 25 C.

This drug is unusual in that it possesses a low order of in vitro activity as measured in commonly used laboratory media, whereas in experimentally infected animals its chemotherapeutic effectiveness compares favorably with commercially available antiibotics.

Preliminary work in noninfected animals demonstrated that subcutaneous doses as high as 400 mg./Kg./day and oral doses as high as 800 mg./Kg./day could be given to mice at daily intervals over a six day period without gross signs of toxicity.

The in vivo antimicrobial spectrum of psicofuranine, as determined in the mouse-protection test, compares favorably with chloramphenicol or novobiocin in those experimental infections in which all are active.

The antibiotic was not active against the viruses of influenza, vaccinia, or western equine encephalomyelitis; nor was it active in vivo against *Entamoba histolytica, Trichomonas vaginalis,* or *Nippostrongylus muris.*

Two of the infectious agents controlled by psicofuranine are of great current interest in clinical medicine, viz., enteropathic *Escherichia coli* strains and the "hospital" strains of *M. aureus.* Psicofuranine is active not only against several different strains of *M. aureus* but also against strains resistant to other antibiotics.

It was not possible to induce resistance in *M. aureus* by repeated passage of the strain in psicofuranine-treated animals.

Progestational and Oral Contraceptive Agents

The Syntex group (H. J. Ringold, E. Batres, A. Bowers, J. Edwards, and J. Zderic, *J. Am. Chem. Soc.* 81: 3485, 1959) report two steroid derivatives with extraordinary oral progestational activity in animal Clauberg assays, and inhibition of ovulation in the rabbit in this series of compounds was found to parallel closely the Clauberg assays. With 17 α - ethynyl - 19 - nortestosterone (Norlutin) rated as having an activity of 1, the compound 6-dehydro-6-chloro-17 α-acetoxyprogesterone was 50 times as active, while the compound 1,6-bisdehydro-6-chloro-17 α-acetoxyprogesterone was 35 times as active.

Journal of Medicinal and Pharmaceutical Chemistry

This is a new journal, to be published bimonthly by Interscience, U. S. subscription, $15.00. It looks very good indeed. The editors are Arnold H. Beckett of London and Alfred Burger of the University of Virginia. Volume 1, number 1 for February 1959 has the following table of contents: J. Druey and A. Marxer, CIBA, Switzerland, "Hypotensive hydrazinophthalazines and related compounds"; N. P. Buu-Hoi, Richard Rips and R. Cavier, University of Paris, "A new class of antispasmodics with considerable activity"; C. K. Cain and John Kleis, McNeil Laboratories, Philadelphia, "5-Ethyl-5-(1,3-dimethyl-2-butenyl) barbituric acid, a potent central nervous system stimulant; A. H. Beckett, A. F. Casy and G. Kirk, Chelsea College of Science and Technology, "Alpha- and beta-prodine type compounds"; Duane G. Wenzel and George N. Beckloff, University of Kansas, "Pharmacology of two tetracovalent organophosphorus compounds and their optical isomers"; Carl D. Lunsford, John W. Ward et al., A. H. Robins Co. and Hazleton Laboratories, "Derivatives of 3-pyrrolidinols"; M. W. Klohs, F. Keller et al., Riker Laboratories, "A chemical and pharmacological investigation of *Piper Methysticum* Forst"; Paul A. J. Janssen, Anton H. M. Jageneau, et al., Belgium, "Compounds related to pethidine."

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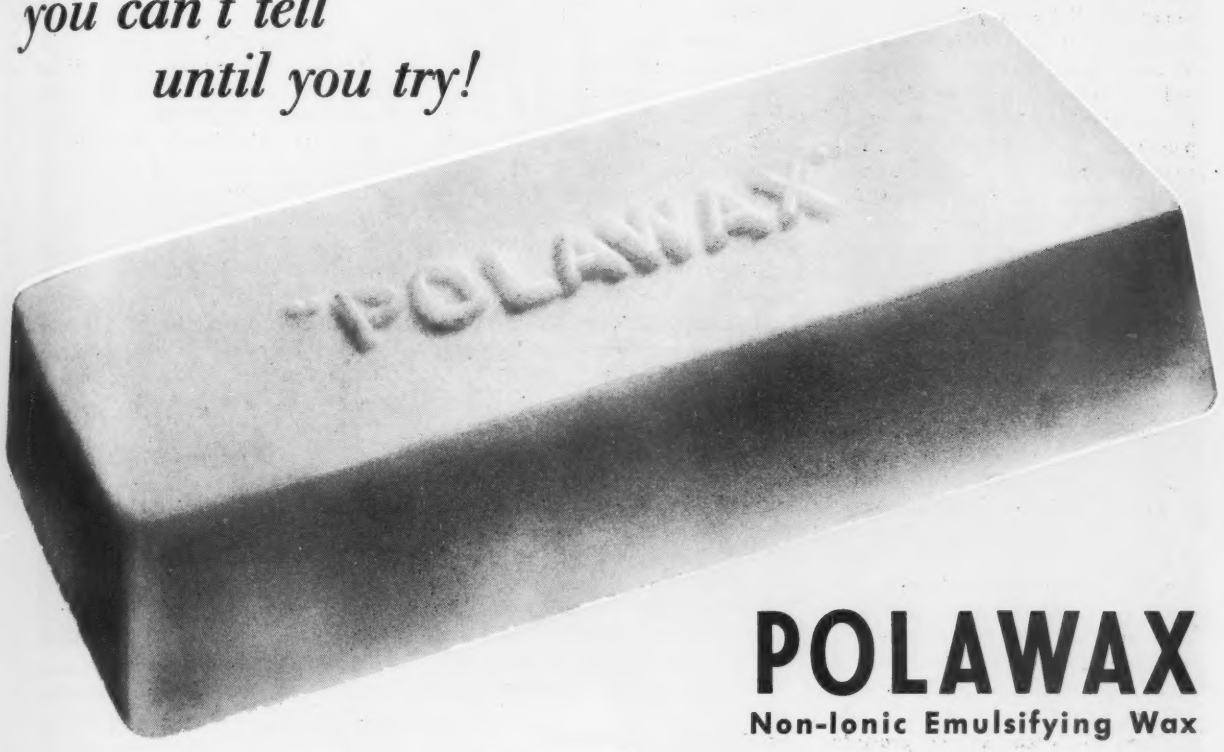

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Royal Jelly Antibiotic

M. S. Blum, A. F. Novak, and S. Taber, III (*Science* 130: 452, 1959) report that 10-hydroxy-2-decenoic acid, component of the lipid fraction of royal jelly, retards the growth of bacteria and fungi. The fatty acid is less than one-fourth as active as penicillin against *M. pyogenes*, less than one-fifth as active as chlortetracycline against *E. coli*, and retards the growth of *Neurospora sitophila* and some unidentified molds. The salt of the acid is considerably less active than the free acid. The free acid was obtained by freezing freshly collected royal jelly, lyophilizing to a powder and extracting with ether. The ether solution was extracted with 2N potassium hydroxide solution and the alkaline solution was made acid to give 2.59 grams of a yellow gum (from 90 grams of frozen royal jelly). Recrystallization from diluted alcohol gave crystals which were identified as 10-hydroxy-2-decenoic acid. All other fractions were inactive against test organisms.

Comment: Synthetic production of this unsaturated hydroxy fatty acid should not be unduly difficult; the acid and its derivatives may prove to be as useful as undecylenic acid. Activity one-fourth as great as penicillin is by no means negligible and may well repay investigation.

Oral Antidiabetic Patent

A British Patent, number 808,071, dated January 28, 1959 has been issued to Farbwerke Hoechst A.G. covering sulfonylureas to lower the blood sugar level on oral administration. The patent broadly covers compounds of the general structure $R'R''C_6H_4SO_2NHCONHR$ in which R is an aliphatic or cycloaliphatic hydrocarbon radical with from two to eight carbon atoms, and R′ and R″ each represent hydrogen or an alkyl or alkoxyl group containing up to six acarbon atoms. This seems to be the underlying patent covering tolbutamide, but not chlorpropamide or carbutamide.

Trifluoromethyl and Sulfur Tetrafluoride

The availability of sulfur tetrafluoride, SF_4, in development quantities has been announced by the Dyes and Chemicals Division of E. I. duPont de Nemours & Co., Inc. This reactive gas is able to bring about the direct replacement of oxygen by fluorine, greatly facilitating the preparation of various types of fluorine derivatives. Fluorine derivative preparation is currently enjoying a vogue in steroid and medicinal chemistry and the game of atom permutation and combination will be made a bit easier in these fields. "Fluorination reactions of sulfur fluoride" are described by W. C. Smith, et al. in a communication to *J. Am. Chem. Soc.* 81: 3165, June 20, 1959 while the application of the trifluoromethyl group in medicinal chemistry is reviewed by H. Yale in *J. Medicinal and Pharm. Chem.*, April 1959.

Tennecetin Antibiotic

A new polyene antifungal antibiotic, called tennecetin, has been isolated by J. Burns and D. F. Holtman (*Antibiotics and Chemother.* 9: 398, 1959). It has a wide antifungal spectrum but it is too toxic for systemic use. It may be of value for topical treatment of fungal infections and appears to be poorly absorbed from the intestinal tract.

Peptic Ulcer Inhibition

J. C. Houck, T. Lee, and J. Bhayana of the Surgical Research Laboratory of Georgetown University Hospital in Washington, D. C. reported to the Division of Medicinal Chemistry at the Atlantic City meeting of the American Chemical Society in September 1959 that carrageenin, a seaweed sulfated polysaccharide, is a competitive inhibitor of the proteolytic activity of pepsin. Addition of carrageenin to the water of fasting rats prevented ulcer formation when they were chronically treated with massive doses of cortisone or the pylorus was ligated, treatments that cause the deevlopment of ulcers. Furthermore, six out of six dogs after one month of histamine dosage were dead of penetrating peptic ulcers; six similarly treated dogs permitted to drink carrageenin-water solutions were still alive. Analysis of canine gastric contents showed that peptic activity was markedly reduced for a number of hours. No clinical data are as yet available.

Comment: If these results can be verified clinically, we can expect many antacid preparations, tablets and liquids, to be formulated with Irish moss and its extractives. The A.C.S. abstract does not provide dosage information.

Aspirin Anhydride

This is another of those bright ideas that is obvious *after* the other man mentions it. Edward R. Garrett of The Upjohn Co. reported to the Scientific Section of the American Pharmaceutical Association in Cincinnati in August and to the Division of Organic Chemistry of the American Chemical Society in Atlantic City in September on various properties of aspirin anhydride. The compound hydrolyzes to aspirin first without losing its acetyl group; it is hydrolyzed by water and acetate and hydroxyl ions. Hydrogen ion does not accelerate hydrolysis. Aspirin anhydride should not produce gastric upset because of salicylic acid production or undissolved aspirin adhering to the gastric mucosa. It should give higher aspirin blood levels than aspirin alone.

Aristomin (Lederle) is a combination of one mg. of Aristocort triamcinolone, 2 mg. chlorpheniramine maleate and 75 mg. ascorbic acid to provide anti-inflammatory, anti-allergic and antihistaminic action. Capsules are supplied in bottles of 30 and 100.

Esidrex-Serpasil (Ciba) consists of scored tablets containing 25 mg. of Esidrex diuretic and 0.1 mg. reserpine and is available in bottles of 100.

Actasal (Purdue Frederick) pediatric drops contain 104.5 mg. choline salicylate equivalent to 1¼ grains of aspirin in salicylate content in each 0.6 ml. Quicker absorption and high salicylate blood levels without side effects are claimed. The preparation is available in 60 cc. bottles.

Glarubin (Massengill) is a crystalline glycoside obtained from the fruit of **Simarouba glauca** and is a specific amebicidal agent for use in intestinal amebiasis. Its toxicity is said to be very low and it is available as 50 mg. tablets in bottles of 40.

Theruhistin (Ayerst), sustained action antihistaminic, contains 24 mg. of isothipendyl hydrochloride and is supplied in bottles of 100 and 1000. It is also supplied as Theruhistin S.A., 12 mg. sustained action tablets in bottles of 100 and 1000.

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(*Continued from page 307*)

Section 526 of the Tariff Act had been intended to be available to "independent" American distributors for the purpose of protecting their investment, but that the privilege could not be invoked where the American distributor was but a "member of an over-all international enterprise."

It might be that even in Judge Edelstein's perfume case decision, a reservation was made with regard to *independent* United States registrants of trademarks affixed to foreign made products, thus giving those of us who have been willing to invest time, effort, and prestige in a territory which had been "virgin" before we created a market, protection against those would try to capitalize on our investment by importing our foreign affiliates' products bearing a trademark which, according to Mr. Justice Holmes' famous opinion in the Bourjois case [*Bourjois* v. *Katzel*, 260 U.S. 689 (1923)], has come to designate and symbolize the American assignee's good will rather than that of the foreign manufacturer. Even the Department of Justice must agree that under existing international trademark law and trade practices, it is possible for a foreign manufacturer to assign, sell, or even license, for a substantial period of time, his potential American good will to an independent distributor here whose only relationship with the foreign manufacturer may consist in receiving certain raw materials or certain finished products from abroad, and in paying a fixed purchase price or royalty therefor, without permitting the foreign manufacturer to exercise any control over the shares in the United States organization or over its management or method of operation. An American assignee who, as in the Bourjois case, has spent a substantial amount of money in purchasing the United States good will and in building it up through his own advertising and promotion to such an extent that the American public will look to him as guarantor of the identity and quality of the product should be held entitled to trademark protection not only against counterfeits but against importation of unauthorized so-called "legitimate" foreign merchandise as well.

While the Department of Justice may understandably desire to remove all international trade barriers resulting from lawful use of patents, trademarks, and copyrights wherever such rights may presently be recognized as having separate territorial existence in each sovereign nation, we all know that promotion of American investment abroad and development of foreign industry in the United Stats through establishment of subsidiary manufacturing units here has been and will be seriously hampered if we were to permit or encourage uncontrolled dumping of foreign-made merchandise through unauthorized sources at cheaper prices in the United States.

Let me demonstrate this by reverting briefly to the recent perfume antitrust suits which resulted in a motion by the government in the Supreme Court to remand the cases to the District Court for the purpose of having them dismissed with prejudice. Judge Edelstein, in reluctantly granting the motion to dismiss, observed that the respondents were to be deprived "of an opportunity to prevail on appeal (an opportunity they are eager to take advantage of) . . ." [*United States of America* v. *Guerlain, Inc.*, 172 F. Supp. 107 (1959)]. In the briefs filed by all three respondents in the United States Supreme Court, they vigorously denied being part of "overall international enterprises" and that they were eager to persuade our highest court that they were in all important respects in the position of "independent" distributors for whose protection Section 526 of the Tariff Act had been specifically enacted.

In considering the economic and legal aspects of the perfume cases, let us treat first the "monopoly" charge and then proceed to discuss the trademark and unfair competition aspects of the case.

The Alleged Monopoly

Judge Edelstein, in finding the respondents guilty of monopoly, came to the startling conclusion that merely as a result of the use of trademarks each respondent had "monopolized a relevant market" constituted by each particular trademarked product itself. The Court emphasized "that no quality perfume can be successfully marketed without a famous name. It would appear that to a highly significant degree it is the name that is bought rather than the perfume itself." The Court also acknowledged that "the most important element in the appeal of a perfume is a highly exploited trade name" and that "each line of Guerlain toilet goods . . . constitutes a separate market." The conclusion was then reached that a trademarked perfume in the same price category was not "reasonably interchangeable" for marketing purposes with any of the competing brands in the same price range. The Court observed that "an unexploited product packaged and merchandised without its trademark would have a negligible effect on the sale of the same product, exploited and trademarked, even though the former may be sold at a substantial price differential from the latter."

Assuming all this to be true, only one conclusion should have logically been drawn from these observations. If the success and popularity of a perfume overwhelmingly depends upon public recognition and satisfaction as the result of the United States distributor's promotional efforts, then this newly developed American good will and demand for the product should entitle him to at least the same degree of protection which the trademark of an American-manufactured product enjoys against infringement and unfair competition. Instead, under the rationale of the perfume cases, an American businessman, who with his own capital and at his own risk creates substantial

(*Continued on page 383*)

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Skin Research

Corticoid Acne

ACTH and corticosteroids may cause sebaceous gland enlargement in suitable human subjects, namely in prepuberal males and postpuberal females, according to J. S. Strauss and A. M. Kligman (*J. Invest. Dermatol.* 33: 9, 1959). In the former the normal androgenic stimulus is negligible, in the latter it is less than maximal. On the other hand, the androgen stimulated glands of post-puberal males are already of maximum size and cannot respond further. Relatively small quantities of androgen (i.e. 5 milligrams of methyltestosterone orally), are capable of promoting glandular enlargement in females and prepuberal subjects. ACTH caused enlargement more consistently than hydrocortisone.

Animal studies already performed by others have indicated similar changes. Corticosteroid-induced acne is essentially the same as acne vulgaris and evolves in the same manner. Sebaceous hyperplasia is the primary event in both. Hyperkeratinization follows the glandular hyperplasia, and if the patient is susceptible, inflammatory acne results. However, there are some clinical differences.

Topical Anesthesia

Work with experimentally induced pruritus by S. G. Macris, I. H. Blank, and H. K. Beecher (*J. Invest. Dermatol.* 33: 15, 1959) seems to indicate that topically applied antipruritic agents do not alleviate the pruritus. Under these conditions, they are unable to alter the end organs' reception of, or reaction to, the pruritic stimulus. If this is true also for the action of antipruritic preparations on itching skin diseases, then any effect they have is probably a psychological one. The patient's pruritus is relieved because he expects relief. This hypothesis could be supported or refuted by a study of the effectiveness of antipruritic agents on pruritus of pathologic origin, using the same method for the study of the effectiveness of antipruritic agents against experimental pruritus. For such a study, the use of adequate controls and placebos will be essential.

Recording Sensible Perspiration

The objective of this study by W. J. O'Malley of the Medical College of Virginia and J. E. Christian of Purdue University, presented before the Scientific Section of the 106th A.Ph.A. convention, was to develop a continuous recording, *in vivo* method of measuring sensible perspiration over a limited area. The study required the design and construction of a suitable electrical circuit and electrolytic cell containing a methanol-acetone-oxalic acid mixture which was sensitive to small amounts of water. The immediate desired application was for the evaluation of antiperspirant preparations. The perspiration was collected by passing dry nitrogen gas through a skin cell which enclosed a small area of skin and delivered the moisture-laden gas to the electrolytic solution. Two such systems were combined through suitable electrical connections to compare simultaneously and continuously normal skin with 24 per cent w/w $Al_2(SO_4)_3 \cdot 18\ H_2O$, three commercial bases and seven commercial products.

Phenolated Scalp Oil

The value of mineral oils containing phenol for the treatment of various common disorders of the scalp, especially psoriasis, has been shown by Vickers, Sulzberger and Obadia, and recently, by Goldberg and Barnett. These materials are easier to use than messy greasy ointments. The difficulty has been to obtain a stable, homogeneous suspension of phenol in the mixture and also a cosmetically suitable material. An improvement over the older phenolated oil mixtures according to L. Goldman and R. H. Preston (*A.M.A. Arch. Dermatol.* 80: 222, 1959) has been developed recently by the addition of surfactants to a vehicle of oil derived from lard instead of from mineral oil. This makes for a stable suspension. The mixture is also perfumed. Because of the recent interest in the disturbed protein metabolism of the epidermis in psoriasis, an acylated amino acid has been added to the mixture. The concentration of phenol is approximately 2 per cent. A medication for psoriasis must be. The material has been put on thick spots of psoriasis on the body, psoriasis of the palms, and around psoriasis ofthe nails. In this latter condition, the phenolated oil is employed primarily to keep the skin about the nails soft.

It can be used also for seborrheic dermatitis of the scalp of the dry type but not for acute seborrheic dermatitis. In senile pruritus of the scalp, this oil may be spotted on sparingly as desired by the uncomfortable patient. This material can be used also as a hair dressing in psoriasis of the scalp.

Pro-Blem (Hoyt Pharmaceutical) is a solution of 70 per cent isopropyl alcohol containing 0.1 per cent of hexachlorophene and 0.5 per cent of cetyl alcohol for the treatment of acne. Sold in 4 ounce squeeze plastic bottles.

Pheny-PAS-Tebamin (Purdue Frederick) is the phenyl esyer of p-aminosalicylic acid, available as a chocolate-flavored powder or as half-gram tablets. The drug is intended for the treatment of active pulmonary tuberculosis.

(*Continued from page 380*)

independent good will here, is treated as "a second-rate citizen," as Professor Milton Handler so clearly put it in a recent address, "Trademarks—Assets or Liabilities?" (48 TMR 661 June, 1958).

Let us consider what will remain of the perfume importers alleged monopoly after you consider some of the actual uncontroverted facts as established by the record in the perfume cases:

(1) The Court itself stated: "About 90 different manufacturers sell over 408 perfumes of different names in the United States, and of these manufacturers, 61 sell toilet good in the same price range as the toilet goods sold by the defendants."

(2) Nine entirely new manufacturers had entered this particular price range since 1946.

(3) There never was an understanding among any of these domestic competitors with regard to price, production, or territory. The Government did not even allege a conspiracy with the distributors' foreign affiliates.

On the contrary, the record shows that there is a continuing and vigorous competition between importers. As a typical illustration, it became necessary for the distributors long ago in their fight for the limited shelf space available in prestige stores to offer dealer cash discounts, to pay salaried demonstrators and to make every possible effort to create a favorable atmosphere toward their line of products.

(4) About 75 per cent of our industry's products are sold as gifts. It is generally understood that in our industry a reduction in price of a prestige item would not necessarily result in an increase of sales from a competitive point of view. It has been correctly observed that "what a buyer of toilet goods really wants is not price competition but the prestige which attaches to higher cost perfume." [Note, 67 Yale L. J. 1110, 1115, n. 14 (1858)].

(5) In view of the fact that there are at least 407 other competitive brands on the market, it is clear that in the battle for survival and expansion a very substantial amount of money has to be spent for advertising and promotion purposes. A study made by the Psychological Corporation some years ago found that 48 per cent of women who bought perfume as gifts made their decision as to brand and fragrance "*after getting into the store*" and that the corresponding figure for male purchasers would even be higher. Consequently, it becomes essential to provide financial incentives to retailers to sell our brands in addition to very large amounts of money invested in general advertising.

The result of all this competition has been that perfume importers in the United States have to be satisfied with a rather slim profit margin.

The Trademark Aspects

But the respondents in the perfume cases, as well as all of those who import ingredients or finished products, were even more alarmed by the trademark arguments that were presented by the Government (these are to an even greater extent now reflected in the Celler bill). According to the Government, a product purchased abroad and bearing the foreign manufacturer's trademark must necessarily be considered under all circumstances a "legitimately" marked product as far as the American public is concerned. This assumption, in my opinion, is contrary to both fact and law. As a matter of business reality, permit me to point to the following established facts:

Only a very small percentage of perfumes is imported in finished form and in the original package. By far the greatest percentage of products sold by the respondents in the perfume cases under their respective trademarks were products which—under the rules laid down by the Federal Trade Commission and by our courts—must be considered American products, since only certain raw materials are imported, to which alcohol and other elements are added in the United States. In addition, our own company and many of our competitors offer products on the American market under our own designs, packaging and control which are not offered on the European and other foreign markets at all.

As a matter of law, it would seem clear, therefore, that many of the more important trademarks used in our industry today reflect the good will, prestige, and guarantee of an American manufacturing or distributing concern, just as it has been found to be true by the Supreme Court in its famous Bourjois decision. In other words, to a large extent the present fame of the name Chanel and of others outside the United States is an instance of "reflected glory" of the good will created on this side of the ocean rather than in France.

It should not be denied, therefore, that our industry needs protection against unauthorized importation of products marked with our trademarks abroad because we cannot otherwise be certain that the American public will purchase an article of the same type, presentation and quality, which as a result of our independent efforts it has a right to expect. I might also mention in passing that, if this were not so, we would find ourselves on the horns of a dilemma, since only recently the Federal Trade Commission once more unequivocally ruled—and was sustained by the Court of Appeals for the Second Circuit—that a cosmetic which is not imported from abroad in its entirety, but to which alcohol or other substances are added in the United States and which is packaged here, must be advertised to the public as an *American* product, even though its basic ingredients may have been imported from a foreign country [*Harsan Distributors, Inc., et al* v. *Federal Trade Commission*, 263 F. 2d 396 (1959)].

Perhaps I have succeeded in these few observations in convincing you that those of us—in my industry

(*Continued on page 415*)

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sicians become specialists, it is increasingly important that we pinpoint our promotion through special mailing lists, by advertising in specialty journals, and by having our professional service representative use discrimination in the selection of products to be detailed. This is both to avoid waste and to avoid burdening the busy doctor with products for which he has little or no use. In recent years we have learned a great deal about how to be selective in our promotion. We still have a lot to learn.

As we pinpoint our promotion more effectively, it may follow that we concentrate more and more advertising and selling effort on the physicians who are our best prospects. With so many companies offering so many products, all competing for the physician's time and attention, we are already accused of over-promotion. This, I suppose is a matter of definition.

I have said that the physician is our customer, but in another sense the patient is our customer, for without patients there would be no prescriptions written and no sales made. Last year, the prescribing doctors wrote perhaps three hundred million new prescriptions. I know of no figures on the number of individual patients involved, but it seems reasonable to assume that it may have been about one hundred million. If we think of the physician as our customer, our market is small numerically, but our potential sales per customer are so large as to justify a very considerable promotional effort.

If we think of the patient as our customer, we are able to reach this tremendous population by concentrating our efforts on the relatively small group of physicians.

An interesting comparison between advertising to the medical profession and advertising to the general public can be found in the relative cost of magazine space. At the most favorable rates a one-page, black and white ad can be placed in four medical journals, at a total space cost of just under three thousand dollars. These four journals, with a total circulation of over six hundred thousand copies, give very complete duplicated coverage of their market. However, if we wish to advertise to the layman, single black and white pages in *Life*, *Time*, *The Saturday Evening Post*, and *The Reader's Digest* would cost in excess of $80,000. The four lay publications, in spite of a total circulation of twenty-six million, would fall far short of covering the consumer market.

Just as our universe of physicians is clearly defined, so, thanks to pharmacy laws and licensing provisions, is our universe of retail pharmacies. Furthermore, American pharmacy has the happy custom of maintaining a complete and systematic file of scripts in the prescription department. (Did you know that in some parts of the world the script is handed back to the patient together with the medication?) All of this makes marketing research—particularly those studies concerned with measuring the flow of drug products—relatively easy for us. How fortunate Dr. Gallup would be if his sampling problems were as simple as ours.

The prescription audit is probably the one type of pharmaceutical market research with which you are most familiar, and I am sure that many of you participate either in David Stiles' studies or in the R. A. Gosselin audit. There are many others, but most pharmaceutical companies rely either on the Gosselin study or on the one conducted by Market Research Associates, which is more commonly known as the Knox Prescription Study. Using well-designed samples of a few hundred stores, either of these services is in a position to give its subscribers a useful measure of the total number of new prescriptions being written each month for all significant products, together with information on prescription sizes, prices, and refill rates.

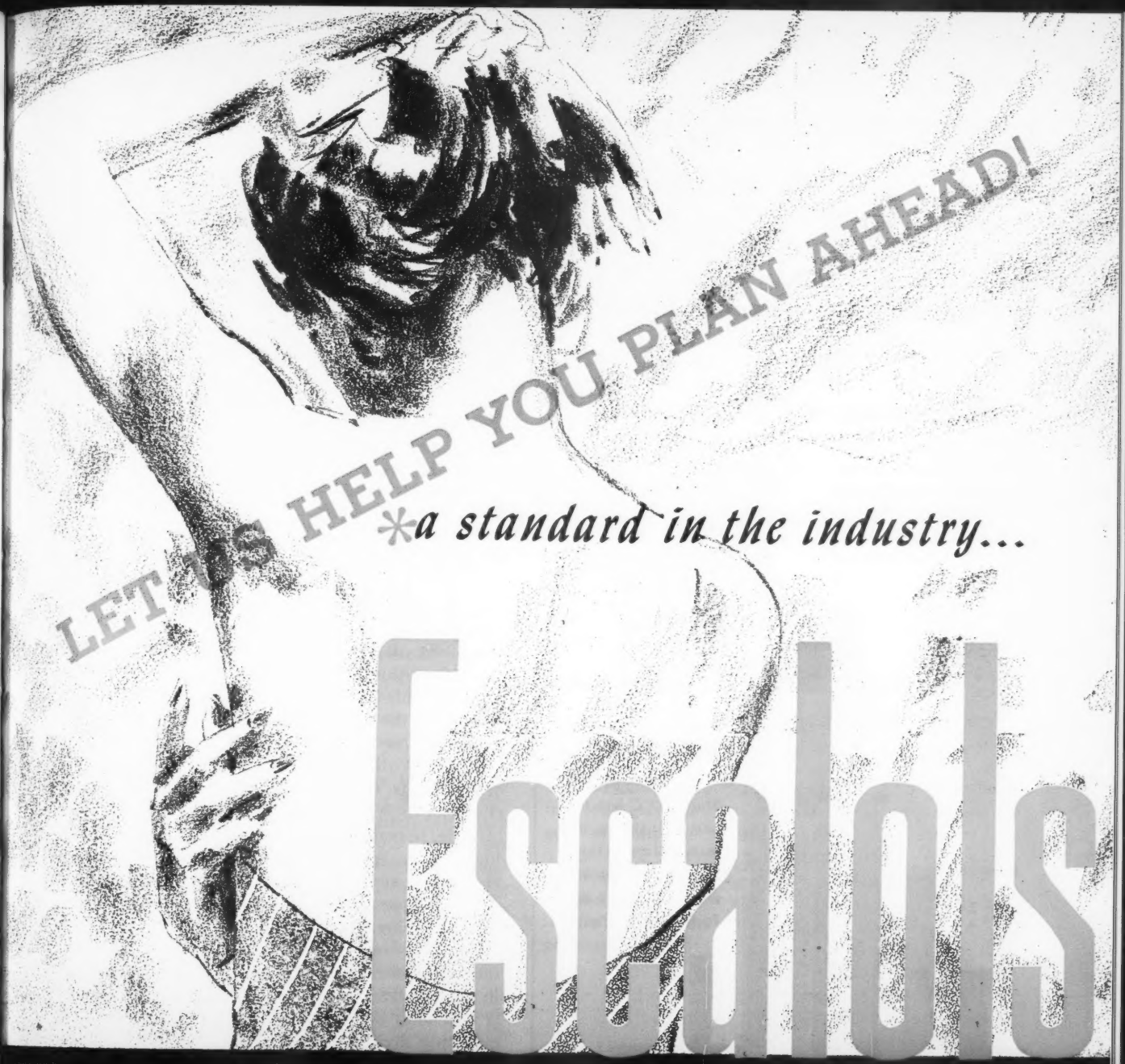
The prescription audits are tremendously useful to us in our market planning. They give us a good approximation of existing markets and of competitive successes or failures. They reflect trends in the acceptance or decline of individual products or types of medication. Incidentally, they are more sensitive and more reliable in this area than are our own sales figures, for a product can coast along on refill business after most physicians have abandoned it. They tell us which forms or strengths are moving. They help in determining dosage forms and package sizes. And, last, but perhaps not least, they help to satisfy the natural curiosity of the marketing man and to give him a better feel of what is going on in the industry.

Generally speaking, this type of marketing research is best done by an independent research agency rather than by the individual companies. It is more efficient and prevents needless duplication. Also, the research agency serves as a buffer between the prescription file and the manufacturer, thus removing any question of violating the confidential nature of the prescription.

Another point at which we are able to measure the flow of products is through auditing of the retailers' purchase invoices. For example, Davee, Koehnlein & Keating, in Chicago, photographs invoices in a well-designed national sample of retail pharmacies each month. They extend the sample data to a national estimate, and provide those manufacturers who subscribe to the service with very complete reports which are classified by product group, by individual product within each group, and by form, strength, and package size where this additional data is desired. This same organization offers a similar purchase audit report for the hospital market.

Here again we are able to detect trends, and it is particularly revealing to see whether sales of a new

(*Continued on page 391*)



*a standard in the industry...

Escalols

...the leading sunscreens

* *Escalols have achieved this pre-eminence by the most exacting of all tests — the use test.*

Millions of satisfied users have proven that suntan preparations containing Escalols give the most dependable protection in the sun and promote a beautiful tan.

SINCE 1904
Van Dyk
BELLEVILLE, N.J.

VAN DYK *and company, incorporated*
BELLEVILLE, NEW JERSEY

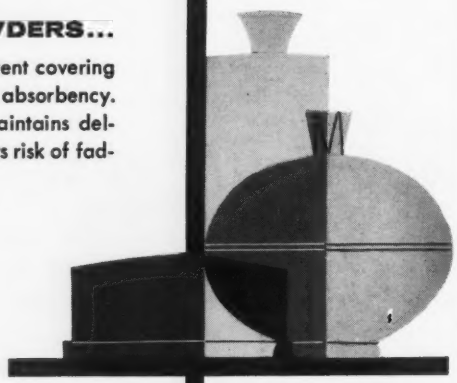
NEW YORK • CHICAGO • LOS ANGELES • TORONTO

SPECIFY STURGE

precipitated
calcium
carbonate
u.s.p.

FOR POWDERS...

You get consistent covering powder and absorbency. Sturge PCC maintains delicate scent, cuts risk of fading colors.



FOR FILLERS...

Sturge PCC has the best consistency and texture for extending or pigmenting creams, lipsticks, or facial preparations.

Since 1823, Sturge has manufactured fine chemicals. Their laboratories are always available for studying any customer's problems. For a sample of Sturge PCC and further information, contact H. J. Baker & Bro.

Manufactured by
JOHN & E. STURGE LIMITED
Wheeley's Road
Birmingham 15,
England

Exclusive Distributor:
H. J. BAKER & BRO.
600 Fifth Avenue
New York 20, New York

Branch offices: Chicago · Atlanta · Savannah · Tampa

Established 1850

(*Continued from page 309*)

and were really marketing departments for areas outside the United States. In fact, in some companies the foreign department reported to the top marketing executive.

Now, however, foreign marketing is undergoing a tremendous transition. It is no longer possible to export to most of the important foreign markets, due to import restrictions, duties, and local competition. Accordingly, most companies have built and are building plants in important foreign markets. Consequently the manufacturing function is becoming as important as the selling function. The fact that good research can be done in a number of countries outside the United States at a cost much lower than comparable work done here is prompting a number of companies to add this third line function within their foreign divisions.

Figure 2 illustrates the kind of complex, highly diversified organization that many of our pharmaceutical houses have become. This company is set up on a product grouping, rather than a functional one, with principal line divisions devoted to the development, manufacture and sales of a definite product class. Our parent company, Miles Laboratories, is typical of this kind of operation, although it is not as complex as the one illustrated in the figure. Note that I have interposed a new top executive, whom I have termed executive vice-president, between the president of this company and the vice-presidents in charge of its operating divisions. This man, whatever his title, is really the chief operating officer, and his function is to coordinate the operations of all these divisions and keep the chief executive officer informed of over-all progress, principal problems, and the like. The chief executive officer has certain top-level staff departments reporting to him also. I have purposely somewhat simplified the staff at the corporate level in this illustration, because the point I want to make is that most of the staff is decentralized into these operating divisions. Each of the operating division heads, usually called president or general manager of his division and also holding the title of vice-president of the parent company, will have line and staff under him comparable to that shown in Figure 1 under the president of the smaller concern. The fact that there would probably be seven accounting departments (one in each operating division and one in the parent company) illustrates what I meant by the duplication of staff in the decentralized company. On the other hand, if a company as complex as this were operated on a centralized basis, the bottlenecks that would develop at the corporate level would not only make it impossible for the operating divisions to operate, but would destroy completely the opportunity to hold the division heads accountable for the success or failure of their operations.

Figure 3 illustrates a very large, non-diversified

(*Continued on page 388*)

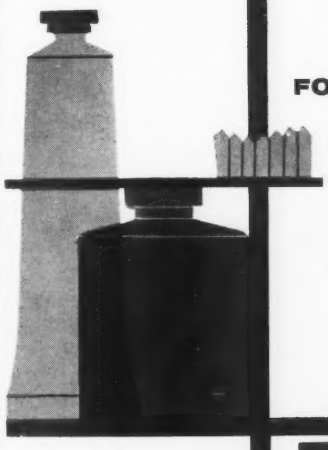
Reader's Questions . . .

Acid Emulsions: *I am having considerable difficulty in changing the pH of some of my creams and lotions to a lower value in accordance with modern ideas of what's best for the skin. Whenever I add acid to the products, they break down completely. Can you give me some ideas as to formulation?*
CHICAGO

I see no reason why there should be any mystery about how to make an acid emulsion. I am afraid there is still too much of classical colloid chemical theory in the minds of younger chemists and not enough appreciation of simple practical factors. An emulsion contains an oil phase, a water phase, and an emulsifying agent or emulsifying system. The emulsifying agent is usually a molecule with a water-attracting portion balanced against a water-repelling or oil-attracting portion; a system will often consist of a mixture of emulsifiers with different water and oil balances. The emulsifying system reduces interfacial tension between the water and oil phases, permitting easier breakdown into small globules; it will coat, in one way or another, globules of oil or of water preferentially and retard recombining of small globules into large drops; it will often increase the viscosity or sometimes give a special structure to the undispersed phase to retard the movement of the droplets. Soaps are the oldest of emulsifying agents and may be alkali metal or amine salts of fatty acids or sometimes of higher acids in some waxes. As with all salts of relatively weak acids, they are broken down by acids, made less soluble by some salts and can undergo reaction with others. In these instances, their usefulness as emulsifying agents is impaired and usually destroyed. This is not the case with a large proportion of modern surface active agents. Instead of soap, use almost any emulsifying agent, anionic, cationic, or nonionic that is not greatly affected by acids, along with a much less water-soluble surface active agent, such as the glycol or glyceryl fatty acids, and an acid-stable emulsion can easily be formulated and prepared.

SPECIFY STURGE

precipitated calcium carbonate u.s.p.

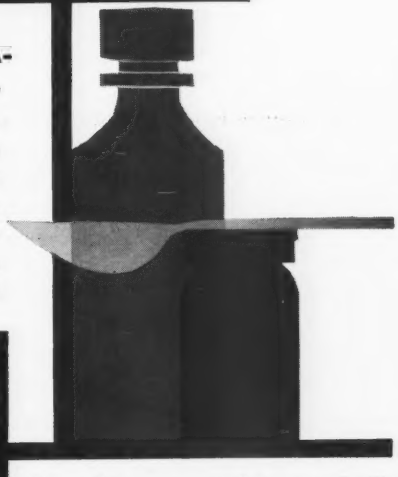


FOR DENTIFRICES...

Sturge PCC forms stable dispersions in glycerine-water mixtures. Gives you a chemically inert controllable polishing agent without taste or grit.

FOR PHARMACEUTICALS...

Sturge PCC is free from taste, gives you uniform texture and a high white color. Recommended for pill and tablet coatings, mixtures and powders.



Year after year, manufacturers of pills and tablets, dentifrices, and cosmetics continue to specify Sturge Precipitated Calcium Carbonate. Sturge PCC, produced by John & E. Sturge of Birmingham, England, has become the standard of excellence. Their experience and careful testing assure PCC of consistent quality—batch after batch.

Manufactured by
JOHN & E. STURGE LIMITED
Wheeley's Road
Birmingham 15,
England

Established 1850

Exclusive Distributor:
H. J. BAKER & BRO.
600 Fifth Avenue
New York 20, New York
Branch offices: Chicago · Atlanta · Savannah · Tampa

(*Continued from page 386*)

company. There would be no point in decentralizing a company of this kind, because it is purely and simply a pharmaceutical house without other divisions such as cosmetics and proprietaries. Therefore, the line at the top is a simple one and reports directly to the president. Since the company is not decentralized, most of the staff is at the top level, and it is easy to see how practically impossible it would be for the president of this company to have four line executives and ten staff executives reporting to him. Therefore, we show the executive vice-president between the president and the chief staff executives, and this illustrates the chief-of-staff concept that is found in American industry. As you can see, the executive vice-president here is literally chief of a large staff of specialists heading up service departments, and, while these departments give their services to the several line departments, it is the chief of staff's function to staff and coordinate these services.

This may be a good place to comment on the terms "decentralization" and "dispersion," which frequently cause confusion in discussions of organization theory. Decentralization means a shifting of responsibility, authority, and accountability down the chart from the top level. In other words, it sets up independent operating entities with an executive in charge of each one. It has nothing to do with geographic location of plants and facilities. Dispersion, on the other hand, has to do entirely with the geographic location of facilities. A large, one-line company such as the example in Figure 3, most often will have plants located in various parts of the country so as to serve regional markets most economically.

Examples of Division Structure

Before going into the structures of the line divisions, I would like to turn back for a moment to Figure 1, which illustrates a medium-sized pharmaceutical company of simple, functional grouping. Let us make the assumption that this company does an annual volume of approximately 30 to 35 million dollars in sales and operates profitably. Figures 4-6 show what is required in the way of organization to carry on this business.

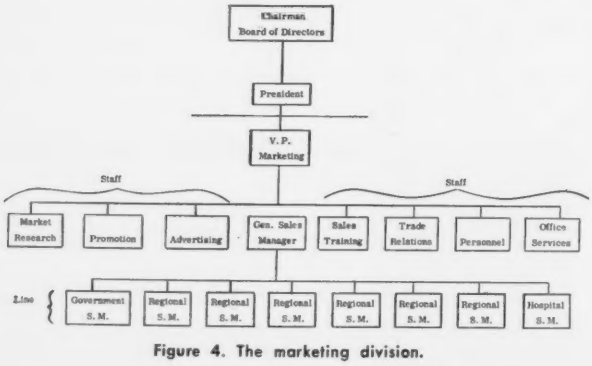


Figure 4. The marketing division.

Marketing Division. First, let us look at the marketing division, as outlined in Figure 4. You will note that I have generally omitted titles, with the exception of those that are well standardized in most pharmaceutical firms. Moreover, space does not permit my going into such details as size or structure of the different staff departments.

The line activities of this division flow from the marketing head to the executive in charge of the field sales force, and thence to six regional sales managers and two sales managers concerned with specific activities—government sales and hospital sales. It is probably safe to assume that each of these regional sales managers has about six district managers under his direction, and each of the district managers will supervise the work of an average of ten regular field representatives or detailmen. This would give us a total of 360 detailmen, plus perhaps ten special field men working under the direction of the sales managers in charge of hospital and government sales. I would guess that this marketing division would have a total of about 380 line employees (not including clerical people) and between 30 and 40 staff members (again excluding clerical help) who would provide specialized services to the line.

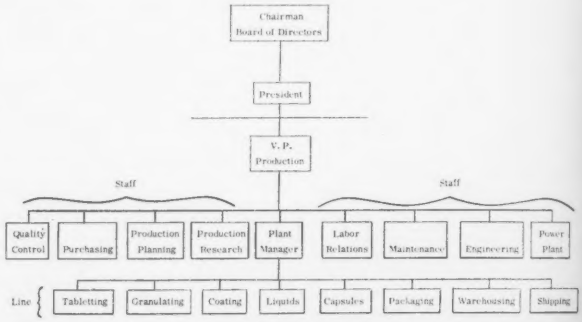


Figure 5. The manufacturing division broken down into its principal line and staff departments.

Production Division. Figure 5 breaks down the manufacturing division into its principal line and staff departments. The line here, as you see, flows directly through the head of the division to the person in charge of manufacturing operations, whom I have called the plant manager. Frequently he is called the chief chemist, although the latter term seems to be falling into disuse. The plant manager has under his direction foremen in charge of the several departments that actually make the company's products, package them and ship them out to the trade.

The head of the production division is assisted by a number of staff departments who help him plan production, control inventory, and so on. He also has departments that render services generally to the manfacturing groups.

Note that Figure 5 shows the quality control department reporting to the vice-president in charge of production, as it is found in a number of pharmaceu-

POLAK'S FRUTAL WORKS INC., MIDDLETOWN, N.Y.

AMERSFOORT, HOLLAND · PARIS, FRANCE · BREMEN, GERMANY · BRUSSELS, BELGIUM · SOFLOR LTD. · PERIVALE, ENGLAND

tical companies. Figure 6 shows it in another division, where it is more frequently found. In some companies, the quality control department reports directly to the president. The reason for this lack of uniformity is the fact that the quality control department performs a function in the pharmaceutical industry that is unique. Since the early beginnings of manufacturing pharmacy, control departments have been given peculiar prerogatives stemming from the life-and-death nature of the industry's products. This

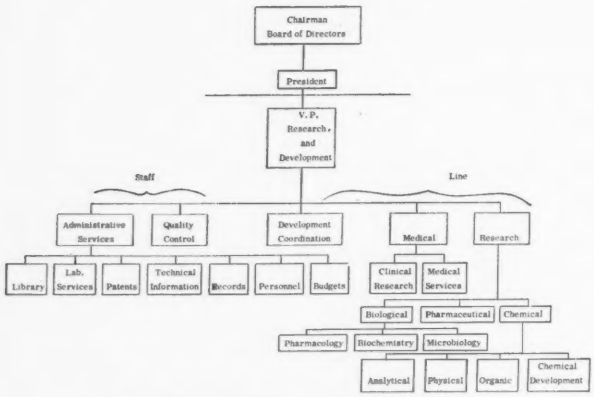


Figure 6. The research and development division.

department has absolute authority to refuse acceptance of a batch of raw material, no matter how hard purchasing has worked to obtain it, no matter how badly manufacturing needs it, no matter how loudly the sales department is screaming for the end product. It has this same absolute power to stop a production batch at any state of manufacture or to condemn finished goods in the plant or warehouses. This is why many different attempts have been made to locate this department so that it cannot come under the influence of the executives most concerned with having finished goods available to meet deadlines. In other words, the industry has historically protected the autonomy of the control department, which, perhaps more than any other single distinction, draws the line between the reputable pharmaceutical manufacturer and the irresponsible parasites on the fringes of the industry.

In the main, pharmaceutical companies tend to have about the same number of production employees as they have marketing employees, with variations depending upon the kinds of products manufactured. In this hypothetical company we are examining, there could be 350 hourly-rated employees. a total of 370 line employees and 35 staff employees in the production division, not including clerical people.

Research and Development Division. Figure 6 shows the research and development division of our pharmaceutical house, and again you will note the separation into line and staff. I believe the formalization of staff functions in these divisions is comparatively recent, with the exception of the very largest firms, but in the past decade, particularly, the unbelievable growth of our research and development operations has caused many scientists to spend many hours working on the organization of their research groups. As an example, the Research and Development Section of the American Drug Manufacturers Association devoted a large part of its meeting in the fall of 1957 to the study of the R&D charts of the member firms, these charts having been collected for the meeting by the Research Administration Committee. Study of the organization charts of the research and development divisions of the 31 firms who participated in this project has shown the enormous variation in organizational structures that exist. Nonetheless, there are many points of similarity.

Many firms have found it useful to create a sort of chief of staff under the director of research and development. Quite often, he is not scientifically trained, but rather has a background of administrative experience. Under his direction are those departments that render services to the groups that are doing research and developing new products.

Note that the quality control department is shown again in this figure, and I think you will find it located under the company's top scientific executive more often than in any other location. While quality control is not really a part of the research and development operation, the desire to remove this department from any influence by the production or marketing divisions very often locates it under the top company executive who, by inclination and training, should be most objective.

The medical department has two key functions. One is to establish the clinical usefulness and safety of new drugs and the other is to oversee the medical soundness and accuracy of marketing activities. In most cases, these two principal functions are reflected in the organizational structure, although they are subdivided in larger firms to a much greater degree than is shown here.

The research line may be subdivided in a variety of ways, depending upon the areas of principal research interest of the individual company. However, in most cases the ultimate division is on the basis of the established scientific disciplines, with these being grouped together according to their primary interrelationships under sub-research directors in the various areas.

In a company of the general size that we are discussing, I think we might expect to find about 60 technically trained line employees and 20 staff employees (not including clericals), but this will vary wildly among different companies, depending not only on the size of the company's research budget, but also on the balance between research work under-

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product hold up in the second, third, and fourth months after introduction. The prescription audit tells us nothing about over-the-counter sales or about the sales of proprietaries. The audit of purchases by retailers does.

Taken together, these two types of market measurement—the prescription audits which concentrate primarily on legend drugs, and the audits of purchases by retailers which cover the entire drug field —give us very good information on the movement, or sales of products. However, they do not tell us *how* the drugs are being used. We still want to know what kinds of patients are being treated with a given compound, and in many cases what the physician expects to accomplish by its use. We want to know the incidence of any particular disease or clinical condition and how the physicians are treating it. In other words, we want to go beyond the prescription and learn about the patient for whom it is written.

These types of information are now available through the continuing physician panel services which are also supplied by independent research agencies. Because I am most familiar with the panel service known as the National Disease and Therapeutic Index (it is usually referred to as the N.D.T.I.), I will speak only of it. First, however, I should mention that there is competition in pharmaceutical marketing research, just as there is in pharmaceutical manufacturing, and that a very similar service is offered by Davee, Koehnlein & Keating. Most members of the National Pharmaceutical Council subscribe to one or the other.

The N.D.T.I. panel consists of a probability sample of over 1200 physicians in private practice, each of whom reports on all patients seen during one 48-hour period in each calendar quarter. Thus we have reports covering nearly 10,000 days of practice per year. By staggering the reporting dates, the agency secures a continuous flow of data which is constantly being edited, coded, and punched into IBM cards for periodic analysis. You can readily appreciate that a tremendous mass of information is accumulated.

Now, what does the physician tell us about the patient? The individual case report form includes: age and sex of the patient; the diagnosis, presenting complaint, or reason for seeing the doctor; where the patient was seen, whether in the office, at the hospital, or on a house call. It also distinguishes between a first visit for the particular indication and continuing care. If any medication is administered, dispensed, or prescribed, it is reported by name, dosage form, and strength. It distinguishes between new treatment and continued treatment. And finally, the physician reports the desired action for each drug.

Often the therapeutic action desired can be deduced from the diagnosis but this is not always the

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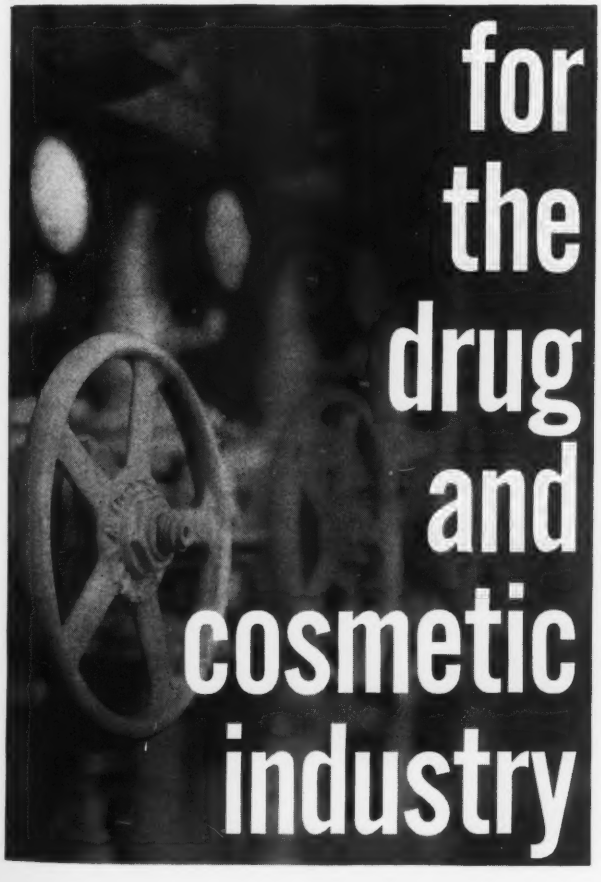

CHEMICAL INTERMEDIATES
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acetic anhydride
benzoquinone
isobutyraldehyde

STABILIZERS
Tenox antioxidants for Vitamin A and such oils and waxes as paraffin, mineral oil and lanolin

PLASTICIZERS
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diethyl phthalate

SOLVENTS
acetic acid
acetone
ethyl acetate
ethyl alcohol
isobutyl acetate
isobutyl alcohol
isopropyl acetate

HEMOSTATIC AGENT and ADSORBENT
oxidized cellulose

MISCELLANEOUS
triacetin
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For samples of these Eastman chemicals, call or write our nearest sales office.

SALES OFFICES: Eastman Chemical Products, Inc., Kingsport, Tennessee; Atlanta, Ga.—3133 Maple Drive N.E.; Chicago (Skokie)—4200 Dempster St.; Cincinnati—1626 Carew Tower; Cleveland—13212 Shaker Square; Framingham, Mass.—65 Concord St.; Greensboro, N.C.—435 Jefferson Standard Building; Houston—1300 Main St.; New York—260 Madison Ave.; St. Louis—10 S. Brentwood Blvd. West Coast: Wilson Meyer Co., San Francisco—333 Montgomery St.; Los Angeles—2060 S. Garfield Ave.; Portland—520 S.W. 6th Ave.; Salt Lake City—73 S. Main St.; Seattle—318 Queen Anne Ave.

Eastman CHEMICAL PRODUCTS, INC.
KINGSPORT, TENNESSEE, subsidiary of Eastman Kodak Company

Trade Literature

Tablets and Capsules

Nysco Laboratories, Inc., 34-24 Vernon Blvd., Long Island City 6, N. Y., has published its Fall-Winter 1959 Catalogue of Tablets and Capsules. The list includes antibiotics, capsules—both hard-shell and gelatin—capsule imprinting and sealing, gum products, narcotic preparations, nasal insufflator, timed-disintegration capsules, powders, tablets and vitamin specialties.

Stress and Circulation

The Wayne County Chapter of the Michigan Academy of General Practice, Detroit, has published the papers presented at its Symposium on Stress and Circulation held in January, 1959. Papers include Studies of Biological Capillary Factors, Miscarriage Prone Pregnancy, Ulcerative Colitis, Evaluation of New Therapeutic Agents, Stasis Dermatitis, Intra-ocular Hemorrhages, and Prophylactic and Therapeutic Measures in Sports Medicine.

Farm Chemicals

S. B. Penick & Company, Farm Chemical and Insecticide Division, 100 Church Street, New York 8, N. Y., has issued an illustrated 40-page catalog covering the products of the division, and including both detailed information on product applications and descriptions of Penick's research and production facilities.

Freeze-Drying

Arthur S. LaPine & Company, 6001 South Knox Ave., Chicago 29, Ill., has issued a second edition of its catalog of laboratory freeze-drying, high vacuum, and related equipment. Illustrated with photographs, the 38-page booklet introduces many new models and lines.

Prescription Pharmacies

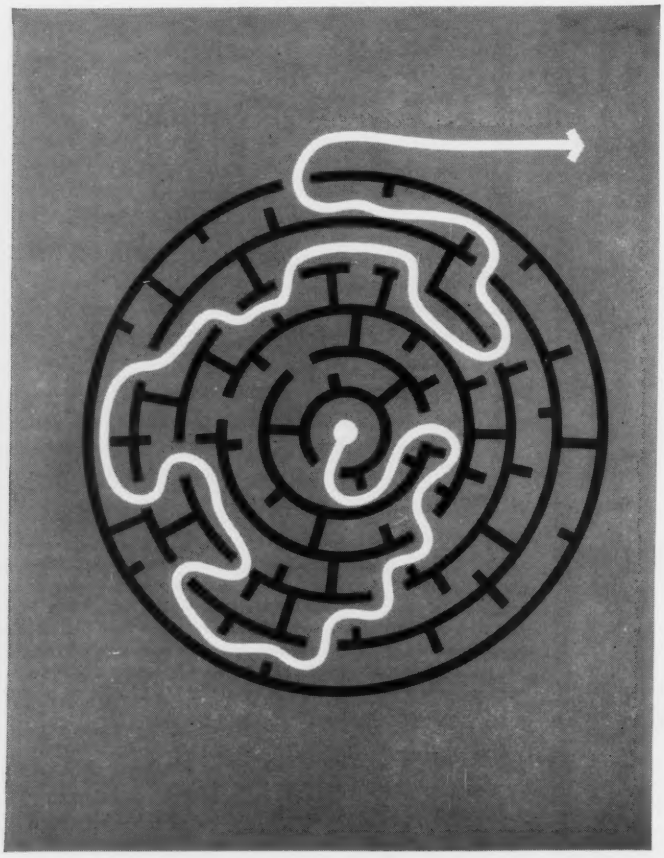
The American College of Apothecaries, Hamilton Court, Philadelphia 4, Penna., has made available a booklet, Facts on the Operation of Prescription Pharmacies, which is a compilation of the operating data of pharmacies operated by the Fellows of the American College of Apothecaries. New features include information on average hours of employment and salaries for prescription pharmacists.

Custom Production Service

Commercial Solvents Corporation, 260 Madison Ave., New York 16, N. Y., has issued a brochure describing its extensive biochemical facilities for custom production. Unit processes available are animation, condensation, esterification, fermentation, hydrogenation, hydrolysis, nitration, oxidation, and reduction. The brochure is entitled, Biochemical and Chemical Facilities Now Available for Custom Production.

Laboratory Sterilizers

The American Sterilizer Company, Erie, Penna., has published a brochure, Laboratory Sterilizers. In 16 pages fully illustrated, it describes laboratory sterilizers and apparatus for industrial and biological research laboratories.



Experienced . . .

with fine chemicals like

MAGNESIUM TRISILICATE (U.S.P.)

In the production of fine chemicals like *Magnesium Trisilicate* we are unexcelled in quality and experience. Our manufacturing process is continuously controlled to insure uniformity and reliability. You can be sure you are always working with the same fine chemical if it is Mallinckrodt Magnesium Trisilicate.

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(*Continued from page 390*)

taken within the company and that carried on outside through research grants and similar programs.

Foreign Division. Since the whole area of foreign operations is in a state of transition, I have attempted in Figure 7 simply to give a candid photograph of a foreign division as it might exist in the midst of this transition.

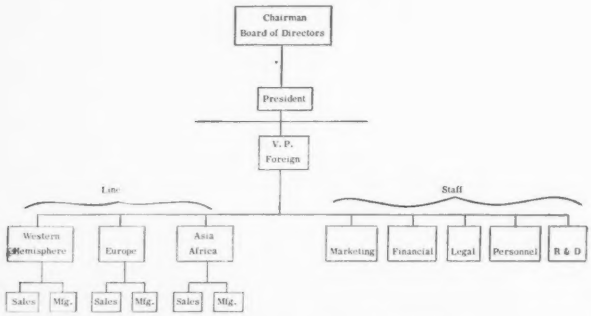

Figure 7. A foreign division in transition.

In most companies, foreign operations tend to be subdivided at the top on the basis of geographical areas, and the subdivisions become greater in number and the areas smaller in size as the foreign business of the company grows. Generally, the line operations of manufacturing and selling are decentralized into these geographical areas, and eventually, research and development will also be decentralized in this manner. Initially, however, research and development is usually a part of central staff, and consists mainly of medical people who perform service functions. As our company develops in its foreign operations, more and more staff functions will be decentralized and placed under the line executives who have charge of operations in the several geographic areas.

Conclusion

While there is no typical pharmaceutical firm and therefore no typical organization structure, I have attempted to show types of structures that are commonly used in the pharmaceutical industry and are typical to that degree.

The present day pharmaceutical company is a product of evolution and, just like an animal, it has developed its own systems and structures that it needs to accomplish its objectives. It is important to remember that we are dealing with one of the most dynamic industries in the world today; so, change is the normal thing. Organization charts tend to become obsolete before they are printed. But sound organization thinking and planning is doing much to help our industry develop as a member of the health team and a significant contributor to the welfare of mankind. •

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(*Continued from page 391*)

case, particularly since we now have many drugs with a variety of actions. Consider, for example, a compound which is useful both as an antiemetic and as a tranquilizer. It may be given to one cancer patient to control vomiting, to another to make his pain less severe, and for a third patient who has neither severe pain or vomiting it may be given to relieve emotional stress.

However, from the data we can learn how a given drug or class of drugs is being used. We can learn the relative frequency with which our sample of physicians sees or treats a given illness. We can learn how the illness is being treated. We can learn the sex and age distribution of patients. And in most cases we can learn the extent to which the condition is treated by specialists rather than by physicians in general practice. In fact, the possible types of tabulations and cross-tabulations are almost limitless.

Obviously, it would be impractical for the research agency to do full justice to the data in routine reports. Instead they supply their clients with basic tabulations—even these are bulky—plus duplicate decks of the detailed IBM cards, if desired. Some clients do the more intensive studies on their own IBM installations while others call on the research agency for special runs. It may interest you to know that in our company we have a file of 200,000 IBM cards representing 1958, and that some segement or other is almost constantly on the machines.

All of this information gives us a much better understanding of current medical practice and is invaluable in planning for new products as well as in establishing marketing strategy for products already on the market.

I have emphasized here only the manufacturers' use of N.D.T.I. data, but the research agency also freely provides the schools of medicine and the various medical societies with special tabulations of interest to them. I understand that this material has been particularly useful in planning the medical curriculums because it gives the professors of medicine better insight into how the private practitioner spends his time.

In mentioning some of the more important syndicated or cooperative services available from independent agencies, I would not wish to minimize the marketing research being done by the individual companies in the industry. All of us are trying to improve our marketing practices. The separate companies have their own marketing research programs just as they have their own programs for scientific research and product development. Naturally, we rely on these syndicated services where possible, but special studies, surveys, and promotional tests are constantly being conducted.

Finally, to illustrate some of the complexities of

(*Continued on page 414*)

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(*Continued from page 313*)

ment of acne by dermabrasion. The talent they embody includes top medical authorities, who lectured before the cameras with interesting visual aids prepared by themselves, with some assistance from the program's producer, Sherman Dryer.

To date, over 100 television stations have used the Schering films, and an estimated 10,000,000 have viewed them. Sam Convissor handles distribution and promotion of the films to stations and interested groups. That the 300 prints of the series are constantly in circulation, can be attributed to their educational and institutional messages. Products are not mentioned in the films.

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Schering's activities on behalf of pharmacists is another area worthy of full description, but that would require an article in itself.

DIURETICS AND EDEMA

(*Continued from page 315*)

of isotonic glucose solution follows a similar diuresis pattern. However, along with mannitol, glucose is rarely used since they are very inefficient. Sucrose has been discarded because of toxic effects on the kidney. Sodium sulfate and sodium phosphate, when given intravenously, are rapidly eliminated in the urine and were occasionally used to abstract water from the body. However, the use of phosphate has been discarded because of the danger of tetany, that of sulfate because of its relative ineffectiveness in promoting loss of chloride and sodium. Urea is still sometimes used in patients with cirrhosis of the liver and congestive heart failure. However, the very large doses needed are very unpleasant, gastrointestinal irritation being added to the bitter taste.

Acidifying Agents

Acidifying salts, such as ammonium chloride, act by a combination of osmotic and acidotic effects. Ammonium chloride is usually given orally in daily doses varying from 3 to 15 grams. The salt is readily absorbed through the intestinal walls and on passage through the liver the ammonium ions are converted into urea, thus freeing the chloride anion. The diuresis induced is mainly due to the excretion of chloride ion in conjunction with sodium. On theoretical grounds, this action should be considered as an efficient form of diuresis and should continue for as long as the acidifying salt is ingested. However, this does not occur. After the second or third day of drug administration, sodium excretion becomes less and less evident and indeed it may reach extremely low values by the fifth or sixth day. Consequently, the diuresis of ammonium chloride is limited to a maximum of three or four days regardless of the dose given. In addition to ammonia, the kidney secretes hydrogen ion which is eliminated in the urine in the form of titratable acids. The excretion of both ammonia and titratable acids continues at a high rate for one to two days after cessation of therapy with the acidifying salt. A "rebound phenomenon" is observed during recovery from the acidosis during which sodium and chloride are retained in an amount which may equal that excreted during the acidotic period. This acidosis is responsible for the rapid loss of effectiveness.

Clinically, ammonium chloride finds use when administered before treatment with mercurial diuretics to raise the plasma level of chloride and thereby increase the effectiveness of mercurial agents. Besides raising the plasma chloride, acidifying salts produce acidosis which favors the excretion of mercury from the body.

Xanthines

The xanthine compounds and their salts have been used for their diuretic activity for many years. They include theophylline, theobromine and caffeine. Theophylline is the most powerful diuretic, but the action of theobromine is more sustained and better tolerated The reports on the mechanism of action of xanthines in promoting diuresis have not been consistent. The most plausible hypothesis is that xanthine diuretics act by depressing renal absorption of water and electrolytes. Evidence is very meagre that there is peripheral mobilization of water or that there is an increased circulatory output with increase in filtration rate.

The diuresis produced by the methylated xanthines is inconsistent and drug tolerance develops. The principal uses for many years was in treatment of cardiac edema and renal insufficiency. This has been largely discarded. The principal diuretic use now is in conjunction with mercurial diuresis, or alone in renal insufficiency, where the effect of the mercurial diuretic on an impaired kidney is feared.

The methylxanthines are only slightly soluble in water. Much effort has been devoted to preparation of combinations with greater solubility. The object is to permit the preparation of more concentrated solutions for parenteral administration and to improve absorbability in the body. More than 50 amines, or alkali and alkaline earth salts of organic acids have been used. At present the most extensively used preparation is aminophylline, the ethylenediamine salt of theophylline. Its diuretic effects, and probably that of other combinations as well, is essentially that of the parent xanthines. A vigorous argument in favor of xanthines is that since many patients with congestive heart failure may also have an anginal syndrome, an effective medication that possesses both diuretic and coronary vasodilator proper-

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ties would be of some advantage. From the pharmacological point of view only the xanthines possess these actions.

In recent years a search for new derivatives of xanthine was undertaken. Numerous related compounds were synthesized and studied. Since the xanthines and other purines may be thought of as fused pyrimidine-imidazole structures it was natural, eventually, that attention should be directed toward pyrimidine and imidazole diuretics. The best results were found in the 6-aminouracils. The most active compounds, with least toxic side effects were Searle's Mictine (1-allyl-3-ethyl-6-aminotetrahydropyrimidinedione) and Rolicton (1-methallyl-3-methyl-6 aminotetrahydropyrimidinedione). Animal studies have shown that these compounds, given orally or parenterally in doses up to one gram, induce a significant increase in the excretion of water and electrolytes. The diuretic effect occurs without any significant change in glomerular filtration rate or renal plasma flow. Mictine and Rolicton appear to inhibit the resorption of sodium by the renal tubules through an as yet unknown mechanism. Both drugs are effective orally, with Rolicton producing less gastric irritation. Oral administration of six to eight tablets to patients with normal and toxemic pregnancies produce an increased excretion of water, sodium, and chloride, which reaches its peak on the second or third day of drug administration. Thereafter the diuretic effects become less and less despite continuation of therapy. This tolerance makes it necessary to administer the drugs on an interrupted schedule. The same is true of the carbonic anhydrase inhibitors. A most interesting feature of Mictine and Rolicton is that drugs can modify kidney resorption of water and salt without the presence of a mercury atom in the molecule, in a manner comparable to the mercurial diuretics. The aminouracils are, however, of little use when drastic diuresis is necessary.

(*This is the first of two articles on diuretics by Dr. Idson.*)

RADIATION STERILIZATION

(*Continued from page 317*)

where enzyme products themselves are considered for radiation sterilization, these factors may be considered as advantages of the radiation technique.

Protection of personnel is another problem which must be considered by a manufacturer using ionizing radiations. An employer who installs a source of radiation must provide adequate safeguards for the people working with the equipment. Such protections as periodic physical examinations, blood counts, the carrying of film badges, and proper shielding of the source must be considered. In many cases, special buildings will be required. With isotope sources, the

possibility of explosions must be very carefullly evaluated and proper safety precautions taken. Insurance agreements and rates are other factors which must be explored thoroughly.

On an economic basis, it seems unlikely that radiation will compete with the conventional heat-sterilization techniques. However, where heat processing is not applicable, radiation costs (compared to filtration techniques, etc.) look more favorable each year.

Types of Radiation and Their Sources

Many forms of radiation exist in nature, or can be produced artificially. To be of practical value for sterilization, however, the radiation chosen must satisfy these requirements:

(1) Availability—sources must exist with adequate output at reasonable equipment and installation cost.

(2) Penetration—the radiation should be able to penetrate the material to be treated and yet should be of a type which is mostly absorbed, so that the radiation energy is efficiently used.

(3) Safety—the radiation should not induce radioactivity in the material being treated. Further, it must be subject to reliable control and economical shielding.

Basically, all radiations can be put into one of two categories—corpuscular (or particle), and electromagnetic. Corpuscular radiation may be thought of as a stream of particles ejected from a source just as bullets are fired from a machine gun. A number of corpuscular radiations can be distinguished from each other on the basis of electric charge and mass.

(1) Heavy Charged Particles. These include protons, or hydrogen nuclei; deuterons, the nuclei of heavy hydrogen; and alpha particles, the nuclei of helium. Although of utmost importance to the nuclear physicist, these particles have little practical value in sterilization because they are comparatively expensive, lack penetration, and induce radioactivity in certain cases.

(2) Neutrons. Neutrons are also heavy particles but carry no electric charge. They are extremely penetrating, but are a very difficult and expensive form of radiation to produce, and usually induce radioactivity in exposed samples. In addition, their penetration is so great and their absorption so low that they are not likely to produce practical sterilization dosage levels.

(3) Beta Particles. These are high-speed electrons emitted by certain radioactive materials in the process of their decay to stable forms of matter. Beta rays are the same as cathode rays, or electron beam radiation, except that betas occur naturally, while cathode rays are machine-produced.

(4) Cathode Rays. Cathode rays are beams of high-energy electrons which are produced in man-made machines. They can be produced with radiation outputs to meet the particular production rates desired.

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High efficiencies are made possible because the radiation is emitted as a narrow beam traveling in one direction, and because the beam can be spread uniformly over the area being irradiated. Cathode rays are the only practical form of corpuscular radiation now suitable for commercial sterilization.

Several machines are available for the production of cathode rays. These include the Van de Graaff Electrostatic Accelerator, the Linear Accelerator, the Resonance Transformer, and the Cockroft-Walton instrument. Basically, these machines consist of a source of electrons and a voltage gradient that accelerate or drive the electrons at extremely high speed through a special discharge tube into the material to be sterilized. They differ chiefly in the method of achieving the high-acceleration voltages.

Within the voltage range of accelerators, the cost of obtaining adequate power for high-volume industrial processing does not appear to be particularly formidable. The smaller units are proving adaptable to low-quantity production techniques and appear to be well suited for installation on conventional processing lines. Higher output machines are also available; however, multiple units may prove to be more economical for many purposes than large very high-power single units. This seems especially true where processing is normally carried out on a number of filling or packaging lines.

A brief analysis of the costs of sterilization using today's accelerator costs indicates that the price per pound of product varies widely, depending on the size of the equipment required for the application and the dosages to be used. Such costs today, including a 5-year amortization schedule, operating, maintenance, and power, range from under 1/10 cent per pound for high-volume, low-dosage irradiation, to about 7 cents per pound for low-volume high-dosage irradiation. Similarly, costs per operating hour range from $8.00 to $36.00, and costs per kilowatt hour from $3.00 to $20.00.

The major element in these costs is the initial capital outlay that must be amortized over the production volume. The cost of power consumed is negligible. Lower capital costs realized as a result of increased production will, therefore, reduce these figures substantially. Electron power at less than $1.00 per kilowatt hour appears to be a possibility within the next few years.

The electromagnetic radiations of interest in sterilization processes include X rays, gamma rays and ultra-violet light. The penetration of U.V. light is so limited, however, that its effects can be considered to be surface phenomena only. For this reason, it has no potential for general radiation sterilization procedures, although it is widely employed as a precautionary device in sterile areas and aseptic packaging lines.

X rays are the form of radiation which is produced artificially by bombarding a heavy metal

target with a beam of high-speed electrons. Considered to be tiny packets of energy (photons), X rays are extremely penetrating but are quite expensive to produce in quantity. In conventional equipment, only a fraction of one per cent of the incident electron-beam energy is converted to X rays—a process much too inefficient for processing applications. Even when very high-voltage X-ray generators are used, this conversion efficiency is still very low. Furthermore, efficient use of even these fractional yields is difficult because X rays can not be focused. While a great number of the early radiation sterilization studies were run using X rays, its potential now seems limited.

This leaves only the gamma rays as useful electromagnetic radiations for sterilization. Gamma rays are fundamentally the same as X rays, except that the name gamma has been given to photons emitted from radioactive materials.

Gamma-ray sources have received major attention in recent years, because this type of sterilization facility would afford an excellent outlet for the growing supply of radioactive isotopes produced as by-products ("waste fission products") during the operation of our nuclear reactors. Some of the isotopes found in these waste fission products include Strontium 90, Cesium 137 and Ruthenium 108. Other isotopes of value for sterilization, such as Cobalt 60, can be manufactured directly in nuclear reactors by bombardment of the element with neutrons.

The economics of isotope sources are also of interest. Based on the present selling price of Cobalt-60 ($2 per curie), an irradiation facility can be designed to operate at about 20 cents per pound. However, the price of Cobalt-60 can be expected to go down in the near future, and irradiation costs of 4 to 8 cents per pound have been predicted. Cost estimates for Cesium irradiation have been placed anywhere from ½ to 10 cents per pound for 2 million rep doses.

While radiation sterilization with gamma rays offers a number of advantages, there are several drawbacks, also. Not the least of these concerns the very expensive and bulky radiation shielding requirements of gamma sources, and the fact that such units cannot be turned off. Safety hazards are also greater in gamma facilities than in cathode ray units.

In selecting a radiation source for sterilization, careful consideration must be given to the penetration abilities of the different forms of ionizing radiation. It is clear, for example, that pharmaceutical materials with considerable thickness will require deeply penetrating radiations in order to insure effective energy dosages at all levels through the product.

On the basis of penetration values, cathode-ray sterilization will usually be feasible only where the sample irradiated is quite thin and has a low density. This difficulty has been circumvented somewhat,

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however, by ingenious equipment design, particularly in the product conveyor units. For example, these units can be arranged so that both sides of the sample are exposed to the radiation either concurrently or in sequence. The effective radiation penetration is thereby doubled.

Gamma rays give much deeper penetration than cathode rays, and therefore can be used to sterilize thicker samples. Because of their specific absorption characteristics, gammas also give more uniform dose distribution throughout the sample thickness.

Radiation Units and Dosimetry

Radioactive isotope sources are usually described in terms of their curie content. The curie is now defined as that quantity of (any) radioactive material which has 3.7×10^{10} atomic disintegrations per second. The curie is essentially a unit of power and is analogous to the kilowatt, expressing, for whatever particular isotope is being considered, the rate of energy release.

Energies in radiation work are expressed in units of electron volts (ev). For convenience, a larger unit, the Mev, which equals 1 million electron volts is often used. One Mev is equivalent to 1.50×10^{-6} ergs.

Power output for X-ray machines and particle accelerators are generally expressed directly in kilowatts. For the usual type of electron accelerator, the power output is in the range of ¼ to 3 kilowatts. Units having much higher outputs are now being constructed; however, the processing rates possible with these units are far in excess of the usual requirements of the pharmaceutical industry.

The basic unit of radiation dosage is the Roentgen. It is the quantity of radiation that will produce ions which carry one electrostatic unit of electricity in 1 cc. of dry air at 0° C. and 1 atm. One roentgen (r) amounts to a *delivered* energy of 83 ergs per gram of air.

The recommended unit of *absorbed* radiation is the "rad," which is equal to 100 ergs of energy absorbed per gram of sample. It is independent of the type of sample or type of radiation.

Two other units are in common use also. One is the "rep" (roentgen equivalent physical) which is the amount of radiation necessary to achieve the same results in tissue as the roentgen does in air. The rep amounts to 93 ergs per gram of tissue.

The "roentgen equivalent man" (REM) has found some use in defining biological effects of radiation in man. It is the amount of radiation that has the relative biological equivalence in man of one roentgen.

Some conversion factors useful in radiation technology are presented in Table 1 (page 404).

Bactericidal Effects of Radiation

The exact mechanism in which ionizing radiations kill microorganisms is not entirely known. Two de-

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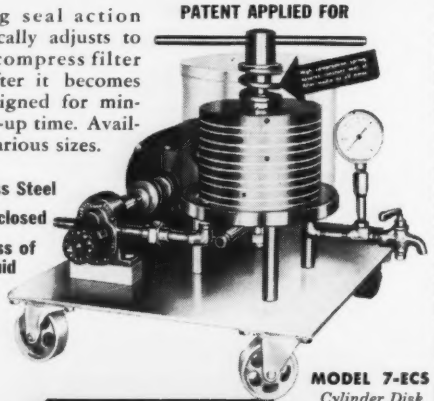

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TABLE 1
Radiation Conversion Factors

1 Roentgen	1 esu/cm³ air NTP
1 Rep	93 ergs/gram
1 Rad	100 ergs/gram
1 Erg	10^7 watt-seconds
1 Watt	70 curies Co^{60}
1 Curie	240 curies Cs 137 3.7×10^{10} Disintegration/sec
1 Mev	1.60×10^{-6} ergs

structive actions are generally thought possible:

(1) A direct hit, whereby the radiation passing through the sample causes an "ionization" in some essential volume of the bacterial cell. The main effect here appears to be on the reproductive apparatus of the cell nucleus.

(2) An indirect effect in which secondary reactions are set up in the cell when the radiation interacts with the surrounding media.

Both of these mechanisms may occur simultaneously in irradiated samples.

For a given radiation dose, the (absolute) number of surviving organisms will be a function of the original bacterial concentration. This means that, in actual sterilization processes, it will be necessary to determine what level of bacterial contamination is present in the samples to be treated. When bacterial contamination is high, high radiation doses will be required. Usually, doses in the range of 1.5 to 2.5 million rads can serve as convenient starting points.

In general, direct hits on microorganisms are believed responsible for most of the lethal activity of ionizing radiations. However, the indirect actions of radiation on the solvent system also have significant effects on microorganisms.

The extent of indirect bactericidal effects in an irradiated sample depends, for the most part, on the conditions of the experiment, and particularly on the environmental conditions of the microorganism. Oxygen tension is a very important factor. For example, *E. coli* is about three times more sensitive to radiation in aerated systems than it is in nitrogenous atmospheres. This observation is of practical significance because, in pharmaceutical systems which can tolerate oxygen, the radiation levels may be reduced sharply if the samples are aerated before exposure.

Decreased kills have been observed when water is removed from samples before irradiation. This is believed to occur because the production of lethal free radicals is minimized in dry samples. Freezing also reduces lethality as a result of the decreased mobility of free radicals in solidified samples.

Another important type of effect is seen with compounds which exert strong protective influence on irradiated bacterial populations. Many of these materials function as (competitive) free radical accepters. With other compounds, the results can be explained more simply in terms of the ability of the protective agent to chemically absorb free oxygen. Sodium hydrosulfite falls in this category.

All the above considerations will tend to modify the effectiveness of radiation procedures. However, the single most important factor governing bactericidal activity is the particular radiation sensitivity of the contaminating microorganism itself.

As a rough working approximation, it has been found that the resistance of a given species of organism to ionizing radiation generally parallels the resistance of that species to conventional heat processing. Thus, spore cells which can withstand high temperatures for long times often are very radiation resistant. Vegetative cells, on the other hand, which are quite sensitive to heat, are usually also quite sensitive to radiation. Exceptions to this rule exist, of course. For example, several species of non-spore-forming bacteria have been isolated recently, which possess very exceptional (high) levels of radiation resistance. Table 2 compares the mean lethal doses for several of the common species of microorganisms.

TABLE 2
Mean Lethal Radiation Doses For Several Organisms

Organism	D_0 (rep.)
Escherichia coli	11000
Aerobacter aerogenes	8000
M. pyogenes var. aureus	33000
M. pyogenes var. albus	21000
Streptococcus faecalis	46000
Serratia marcescens	7000
Corynebacterium xerose	30000
Ps. fluorscens	5000
Ps. aeruginosa	4000
Sarcina lutea	25000
Bacillus thermoacidurans	64000

While a great deal of work has been done in determining the radiation levels required to treat specific organisms, very little has been done with mixed cultures containing multiple species. When this type of contamination occurs in pharmaceutical products, the radiation level will have to be adjusted to inactivate the most resistant species present.

In the over-all picture, it appears that the sterilizing radiation dose depends on many factors, including the type and number of contaminants and the nature of the sample. In practice, therefore, it is absolutely essential that the sterilizing dose for any product be determined by direct experiment under actual production conditions. Local variations in technique or unusual responses of the microorganisms due to the presence of protective agents in the sample can then be recognized. At the same time, some consideration can be given to the particular degree of sterility required in the sample.

Conclusions

Sterilization by irradiation with cathode rays is now feasible and already has been commercially applied. The chief source of such radiation is man-made machines. In coming years, when the radioactive isotopes produced in our atomic reactors become available in large quantities and at low cost, isotope sterilization procedures may become practical and economical.

Many problems in radiation processing have been

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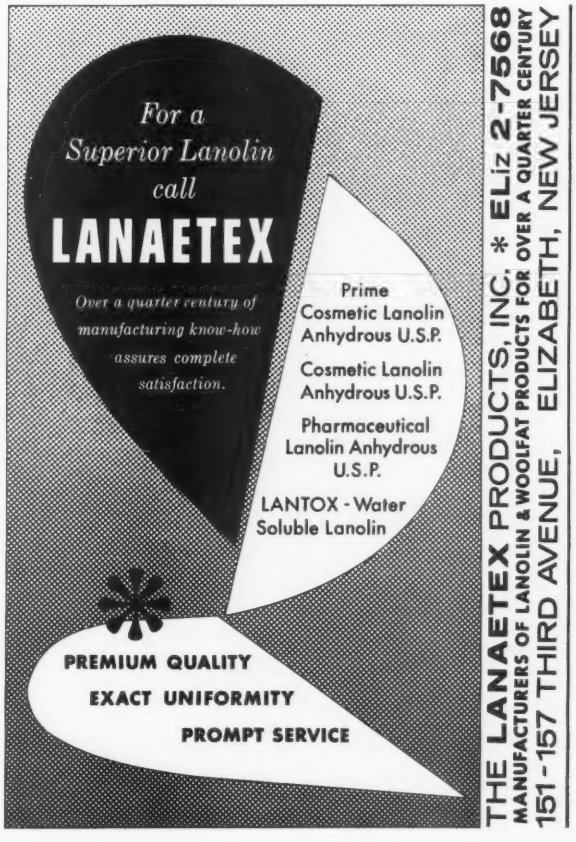
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overcome but many are yet to be resolved. The overall impression is that radiation sterilization will continue to find definite areas of usefulness in the pharmaceutical industry. The fields of applications, however, do not seem quite as broad as they did 10 to 15 years ago.

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TABLET LUBRICANTS

(*Continued from page 319*)

is a good anti-adherent as well as a good glidant. Munzel terms these agents "anti-adhesives" or "anti-sticking" agents and classes solid paraffin, stearic acid, cocoa butter and soaps in the group of com-

TABLE 1

Evaluation of Materials as Tablet Lubricants

(Sulfathiazole granulation made with starched paste and sieved to 8-20 mesh granule size was the standard granulation.)

Material used as lubricant	'R' Value	Ejection force (KG)	Type of lubricant mechanism
Perfect lubrication (hypothetical)	1.00	0	—
Magnesium stearate	.95	8	B
Paraffin*	.96	13	F
Calcium stearate	.94	10	B
Sodium myristate	.91	10	B
Sodium stearate	.91	16	B
Aluminum stearate	.90	18	B
Stearic acid	.90	30	B
Cetyl alcohol	.90	40	F?
Stearyl alcohol	.87	32	F?
Carbowax 4000[1]	.86	38	I
Talc	.85	45	A
Mineral oil* U.S.P. Heavy	.78	44	F
Boric acid	.76	90	A
Sodium benzoate	.72	103	?
Benzoic acid	.71	100	?
Starch 5% (corn)	.70	130	?
Control (no lubrication)	.67	110-170	
Aluminum hydroxide	.66	175	0
Zirconium oxide	.65	158	0
Vermiculite (325 mesh)	.63	182	0
Aluminum oxide	.63	194	0
Magnesium trisilicate	.63	200	0
Zirconium silicate	.63	200	0
Veegum (Vanderbilt)	.62	265	0
Mucic acid	.61	293	0
Silicone resin (XR-102, very fine powder, D. C.)	.60	235	0
Calcium gluconate	.59	291	0

*Lubricant was sprayed on tumbling granulation as a solution.
[1]Registered trademark, Carbide and Carbon Chemicals Company.

pounds having this activity. Thus, some of the better lubricants are considered to have anti-adherent activity. It is common to consider such compounds as the impalpable silicone powders, vermiculite and other silicaceous materials as anti-adherents.

Talc is shown to have only moderate effect as a lubricant in Table 1. Other silicaceous materials were shown to increase friction appreciably at the die wall during tablet formation and ejection. This was a surprising result in view of the smooth, slippery, impalpable nature of these materials. A possible explanation of this was offered recently by Dr. David Train[9] on the basis of relative shear strengths. Lubrication, in the sense of tablet lubricants, appears to be a function of shear strength of the components of the system. If two surfaces of hard texture in relative motion have interposed between them a material of lower shear strength than either of the two surfaces, the interposed material will shear and leave the two opposing surfaces unaffected. On the other hand, if the interposed layer is harder (has a higher shear strength) than one of the materials (the tablet in this case), the interposed layer will remain intact and the softer material will shear and smear along the die wall. A similar occurrence takes place in absence of lubricant when the tablet surface is roughened by shearing away as the tablet is ejected. D. Train found that under pressures comparable to those encountered in tablet making the shear strength of soap-

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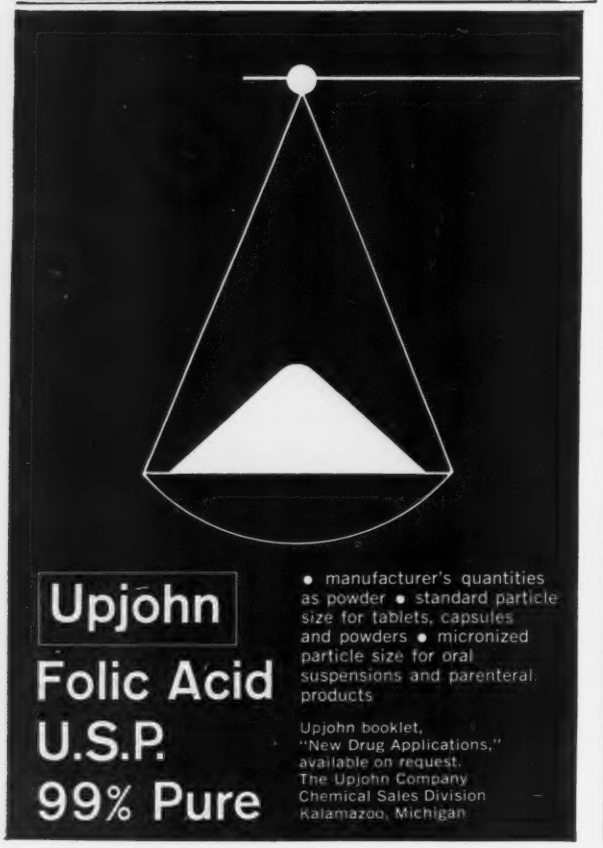
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tone (talc) increased by the order of ten-fold. This means that the shear strength could rise to such magnitude that silicaceous materials under sufficient pressure may not shear, or shear with difficulty, due to the great increase in shear strength. Thus any slipping or shearing would be that of the next softest substance in the system, namely the granules and formed tablet.

This explanation is compatible with the observations of the writer and could account in logical manner for the behavior of such substances as vermiculite and zirconium silicate.

Characteristics of some Common Tablet Lubricants

Table 2 is offered in an attempt to clarify the functions of some common tablet granulation additives.

TABLE 2
Comparison of Activities of Some Common Tablet Lubricants

Material added to granulation	Lubricant activity	Glidant activity (after Munzel)	Anti-adherent activity (estimated)
Magnesium stearate	+++++	—	++
Calcium stearate	+++++	—	++
Paraffin	+++++	—	++
Stearic acid	++++	—	++
Talc	++	++++	+++++
Starch	0	+++++	+++++
Polyethylene glycol 4000	+++	+++	++

Different granulations will react somewhat differently with respect to a given additive; consequently this table is composed on the basis of broad generalities, and should be interpreted in the same light.

Granulation Lubricity and the Water-Soluble Tablet

Many tablets being produced in the drug and food industries are intended to dissolve completely in water. A major problem encountered in their production is one of lubrication or a combination of lubrication and anti-adherence. This problem can generally be approached from several directions, such as:

(1) adapting the compression process to yield suitable tablets while using granulations of recognized poor lubricity;

(2) adding water-soluble materials in an effort to improve granulation lubricity to an acceptable degree;

(3) using tablet dies made of materials possessing intrinsically low frictional properties, which is admittedly a theoretical approach at best;

(4) adding a minimal quantity of a good water-insoluble lubricant to the formulation.

It is a characteristic of friction that the less pressure exerted, the less friction that will be encountered. If tablets can be produced satisfactorily at low pressures the lubricity level of the granulation may be relatively low and still yield reasonably good tablets. Some formulations may be benefited by the addition of water-soluble substances which will improve the lubricity of granulations to the extent that

tableting is possible. In view of the fundamental nature of lubrication it is not likely that highly water-soluble compounds such as inorganic salts and carbohydrates can act as effective lubricants. It may be possible to reach a compromise between water solubility and a reasonable degree of lubrication activity in several new compounds now appearing in commerce. High molecular weight polyethylene or polypropylene glycols added as fine powders may benefit certain granulations; waxy-solid surfactants such as Ethofats (Armour) and Arlacels (Atlas) may also be useful.

Nelson[10] demonstrated that four-fifths of the friction exhibited during the compression of poorly lubricated granulations occurs at the tablet-die wall interface as the tablet is ejected. Therefore, reduction of the surface area of the tablet in contact with the die wall will reduce the total friction created in the process and permit processing of granulations of relatively low lubricity levels. This can be accomplished by the use of deep cupped punches or by making thin tablets of large diameter.

An unpublished study[11] utilized several different metals as die walls. The object was to find a suitable die-wall material possessing a low coefficient of friction which would permit compression of tablets without the use of lubricants. The metals used were steel, brass, chromium, copper, silver, aluminum, cadmium and zinc. The friction was roughly the same for all these metals, being somewhat less in the case of copper and silver. The only die-wall material to show appreciable reduction of friction was the silver die amalgamated with mercury and rubbed to a good polish. This amalgamated die was resistant to the wear of the test compressions. Perhaps further study in this area might yield a die wall that was sufficiently wear-resistant and frictionless to permit the manufacture of suitable tablets without lubricants.

It would appear that a combination of these factors could assist the tablet formulator in developing trouble-free, elegant, water-soluble tablets. However, in the event that none of these methods yields suitable tablets it may be necessary to resort to the addition of a minimal quantity (1/10 to 1/2 per cent) of magnesium stearate or other excellent, but water-insoluble lubricant.

In summary, materials traditionally added to tablet granulations as lubricants have three actions, two of which may be contradictory for a given compound. Awareness of these functions may help obviate formulation difficulties. The prime deterrent to making water-soluble tablets is inadequate lubrication or a low lubricity level of the granulation. Formulations used to prepare completely water-soluble tablets may represent a series of compromises between efficacy and water-solubility.

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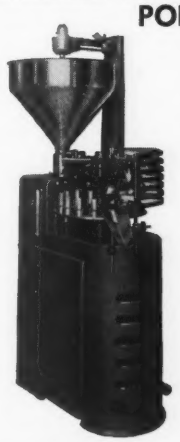

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ESSENTIAL OILS

(*Continued from page 322*)

through several hands before they reach St. Denis. Shippers bulk the small lots to make large lots for export—these latter are then analyzed in the government laboratories. If they are up to standard, an export license is granted. (To pay the expenses of these laboratories, a tax of 1 per cent is levied on the export price.)

With age, the acid number and specific gravity of the oil increase; optical rotation and ester content decrease. In addition there is a color change from straw or green-yellow to brown or reddish-brown. The odor loses its characteristic top note and takes on a resinified character. For these reasons, old oils that cannot come up to standard are often mixed with fresh oils.

Reunion geranium oil is occasionally adulterated with alcohol; such crude adulteration is easily detectable by simple analysis. The more expert kinds of adulteration are unknown on Reunion, since producers and local dealers know nothing of the chemistry of essential oils. Moreover, if the compounds necessary to skillful adulteration (such as, geraniol or citronellol) were imported into Reunion, the suspicion of Customs officials would be aroused at once, because there is no soap, cosmetic, or perfumery factory on this small island that could use such products.

In spite of the superiority of Reunion geranium oil, uncertainties surround its production. In the first place, the crop itself is liable to heavy damage from cyclones. Hurricane winds may blow all the soil away from a hillside, carrying plants with them; or they may rip and tear the plants to pieces. Water can then enter the root systems, and "rouille" (rust) may ensue; the roots rot, overground plant parts can no longer obtain nourishment, and the plant dies. Prolonged rainfall, also, is a danger; sometimes 50 to 75 per cent of a planting may be lost in the course of a few days.

And there is economic uncertainty. As has been said, the oil reaches exporters in St. Denis via a chain of local dealers and agents, including Chinese shopkeepers. The system works like this: when the planting season starts, landowners advance money to their "colons" (sharecroppers) for the preparation of fields,

the cultivation and harvesting of plants, and finally, the distillation of the oil. The end product is divided between landowner and "colon," the landowner receiving one-third of the oil, the "colon" two-thirds. The landowner may then hold his oil for speculation, or he may sell it to an exporter. The sharecropper sells his oil to the landlord (to pay back money advanced earlier in the season), or, more often, to a Chinese shop owner—in the latter case the oil takes on the property of currency, a means of barter against the necessities of daily life. In his turn, the Chinese either sells his accumulated lots of oil to field brokers supplying exporters in St. Denis, or stocks it for speculative purposes.

It is estimated that more than one-half of the annual production of geranium oil is held for such speculation: these hidden lots play a decisive part in determining the price structure of the oil. Many people, even private individuals outside of trade and commerce, engage in speculation in the oil, investing heavily in it. The existence of their hidden stores, which may appear suddenly and unexpectedly on the market, renders it difficult for anyone—even a most experienced exporter—to make predictions as to inventories and prices. There seem to be no secrets on Runion—a cabled inquiry from abroad for a substantial quantity of the oil may upset the market, often to the disadvantage of the foreign buyer.

To counteract this market instability, it would seem advisable for purchasers abroad to channelize their buying through one or two reputable essential oil houses with confidential connections in Reunion. Only in this way can purchasing be made continuously and advantageously, avoiding unnecessary fluctuations.

Oil of Vetiver

Reunion vetiver oil has been on the market for many years and has always enjoyed a high reputation for its quality. Total production of the oil on Reunion now ranges from 20 to 30 metric tons per year, being second now only to that of Haiti in the West Indies.

While the geranium oil industry suffers a great deal from cyclones, that of vetiver is much less exposed to damage by strong winds, for the simple reason that the oil-bearing parts of the plant (i.e., the roots) are underground, and protected. Hence cultivation of vetiver offers fewer hazards than that of geranium.

There are, on Reunion, from two to three hundred growers of vetiver. The plant is grown at altitudes ranging from 1,800 to 2,100 feet; it thrives best in a decomposed volcanic soil, very loose. From this kind of soil the roots can be extracted easily by hand, and none of the fine rootlets remain. Harvest lasts from June to November (the dry season). When the rains fall, later on, the soil turns into mud, and gathering of the roots would be a difficult business. Also,

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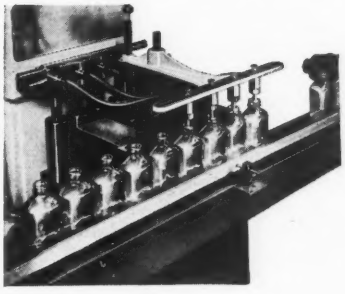

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when the summer rains start, at the end of November, the cycle of vegetation recommences: the oil seems to disappear from the roots, with a resultant sharp fall of yield.

The roots are extracted after one year in the ground. They are pulled up by hand after the leafy overground parts of the plant have been cut off by machetes. Then the root system is shaken, to free it of dirt. For replanting purposes, the root stock is then divided and planted.

Reunion Island has about one hundred vetiver distilleries, including perhaps ten fairly large producers. The stills are bigger than those used for geranium, being generally stationary and housed in some kind of shack. They are heated with direct fire; the wood for this purpose comes from nearby forests. Distillation of one charge takes about 24 hours, because the steam pressure is low. The distillate runs quite warm from the beginning to the end of distillation; this prevents formation of troublesome emulsions. The oil is then separated on top of the oil receiver; two of the latter generally suffice for one still. Five hundred kilograms of vetiver root (not comminuted, but sun-dried) yield from 7 to 8 kilograms of oil.

Properties of the oil depend largely on:

(1) Age of the root material. The longer the root remains in the ground prior to harvest, the higher the specific gravity and optical rotation will be. Oils with these elevated properties, which have a stronger, finer and more lasting odor, are preferred by the trade.

(2) Length of distillation. If distillation is not carried on for a sufficient time, the oil has a low specific gravity and optical rotation. The ester number does not appear to be affected by length of distillation.

In order to raise the specific gravity and optical rotation artificially, Chinese intermediaries often let the oil stand in open cans for two or three months.

The obsolete stills common on Reunion require a lengthy distillation—and hence an expensive outlay of wood. The cost of producing the oil is therefore higher than in Haiti (now the largest producer of vetiver oil).

Like geranium oil, Reunion vetiver oil usually passes through a number of hands before it reaches the St. Denis exporters. Hence it has become an article of speculation, with speculators holding considerable supplies—often for several years—until higher prices prevail and better profits can be made. The oil keeps well, and even improves with age if properly stored.

Every shipment of vetiver oil must be analyzed by the government laboratories in St. Denis before a permit for export is granted. Official specifications are these:

Specific Gravity at 15°/15° C.	0.990-1.015 (temperature correction factor 0.0008)
Optical Rotation at 20° C.	+16° to +25°
Refractive Index at 20° C.	1.521 to 1.530
Acid Number	4.5 to 15 (most American importers will not accept oils with an acid number above 8)

Ester Number	5 to 20 (usually 6 to 8)
Solubility in 80% Alcohol	Soluble in 0.9 to 1.4 vol.

With the passage of time, the specific gravity and the optical rotation of the oil increase.

Oil of Ylang Ylang

The ylang ylang tree was introduced to Reunion Island at the beginning of this century. For many years the island produced substantial quantities of ylang ylang oil—an oil highly appreciated by connoisseurs among the leading perfumers in Paris for its particularly fine bouquet and delightful top note reminiscent of jasmine. However, with Nossi Be (and more recently, the Comoro Islands) entering the market with lower-priced oils, production on Reunion Island has declined in the past twenty-five years, amounting now to a total of about 1,200 kilograms per year. There are now only two producers left (one in Piton-St. Paul and the other in neaerby Pourpier-St. Paul). Their distilleries are equipped with efficient stills yielding these qualities:

Fractions	*Length of Distillation*
Extra	First 2½ hours
Second	Next 2 hours
Third	Final several hours

No first fraction is obtained in the distillation method used by these producers. They start distillation by using direct steam from the very beginning, after having covered the flower material with water.

Each of these distillers produces these quantities of oil:

Quality	*Kilograms*
Extra	200
Second	200
Third	200
Total	600

The specifications of the government laboratories in St. Denis require the following limits for oil of ylang ylang:

Quality	*Spec. Grav. at 15°C.**	*Ref. Ind. at 20°C.*	*Opt. Rot.*
Extra	0.950-0.986	1.498-1.509	—25° to —40°
First	0.932-0.953	1.500-1.509	—33° to —60°
Second	0.922-0.937	1.5057-1.5117	—40° to —68°
Third	0.910-0.920	1.5071-1.5150	—35° to —67°

*(temperature correction factor 0.0008)

Acid No.	*Ester No.*	*Solubility 90% Alcohol*
Less than 2.8	132-162	0.0-2.5 vol.
Less than 2.8	89-130	0.0-2.5 vol.
Less than 2.8	56-89	Insoluble
Less than 2.8	34-60	Insoluble

PATENT THOUGHTS AND TRENDS

(*Continued from page 343*)

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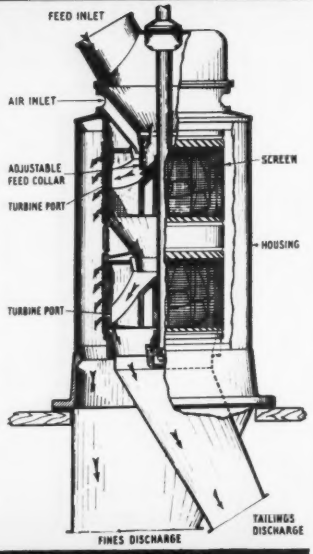

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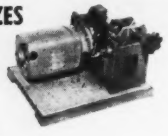

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2,893,918—H. A. Abramson—Deodorant.
2,893,958—44 Trinity Place Corporation—Odor Reducing Composition.
2,893,992—Hoffmann-La Roche — Benzodiazepine 4-Oxides.
2,893,993—G. D. Searle—Aryloxyaralkyl Tetrahydropyrimidines.
2,893,996—W. R. Grace—N-Amino Derivatives of Tropine Alkaloids.
2,893,999—Merck—Dodecahydrophenanthrenes.
2,894,002—Merck—Dodecahydrophenanthrenes.
2,894,006—American Home Products — Testosterone Acetoxy Methyl Pentanoate.
2,894,008—P. B. Sollman—Pregnadiene-3,20-Diones.
2,894,028—W. R. Grace—Cyclohexylideneimino Compounds.
2,894,029-30—American Home Products — Benzhydryl Pseudothioureas.
2,894,033—N.V.N. Comb. v. Chem. Ind. (Netherlands) —Antispasmodic Diphenyl Dialkylaminopropane.
2,894,871—Upjohn—Alkyl Hydrazones of Cycloheximide.
2,894,872—Upjohn — Cycloheximide Keto-Carboxylic Acid Esters.
2,894,874—Commercial Solvents—Cycloserine-Pyridoxin Composition.
2,894,876—American Chicle—Oral Deodorant.
2,894,912—Lever Brothers—Isethionate Detergent Bar.
2,894,948—Ciba — Disulfamyl Benzothiadiazine Dioxides.
2,894,946—Sterling Drug—Aroylmethyl Oxo Dihydro Benzothiazines.

MARKETING PHARMACEUTICALS

(*Continued from page 395*)

our marketing planning, I remind you that we are operating in an increasingly fragmented market. There are no longer panaceas which are good for all the ills of man or beast. Rather we offer more and more specific medications, and each product competes, or will compete, with a limited number of other products in its own area. Last year, in cooperation with the research agencies, a committee of industry marketing research people constructed a classification system oriented to the needs and interests of our marketing people. The result was a list of 45 major drug categories, some of which were further subdivided, to produce a total of 91 classes.

We ordinarily think of a retail drug store as having a prescription department. Did it ever occur to

you that the prescription department itself has 45, or even 91, sub-departments?

The typical company is active in only a limited number of these market segments. This is particularly true of the so-called specialty houses, and even the full-line companies have drastically reduced their catalogs and are tending to concentrate their efforts in selected areas. The modern physician can no longer practice medicine from the catalog of his favorite manufacturer. The reason for this is obvious: real success in our industry comes from the discovery or development of new products. Research is expensive. I know of no company which has the capital, or the facilities, or the scientific manpower to work effectively in all areas at once. Because each company tends to concentrate its research in areas where it has the most experience and the most competence, we often seem dedicated to out-dating our own best products.

LICENSING PERFUMES

(*Continued from page 383*)

and others—who operate independently in the United States, and who even do substantial manufacturing here, need not only the protection of Section 42 of the Trademark Act against counterfeits, but should be held entitled to protect our substantial investment and the integrity of merchandise imported into this country under our trademarks right at the place of first contact with our country, that is, at the Bureau of Customs and at the Ports of Entry.

The Problem of the Returning American Tourist

I am, of course, fully aware that even those who are in basic agreement with this position may question the extent to which Section 526 has been applied in the past, not only with regard to *commercial* importations, but with respect to importation for personal use by returning American tourists. Let me point out that our industry faces a far more difficult problem in this respect than does, for instance, a heavy industry; it is not likely for anyone to bring back to the United States more than one automobile or sewing machine for "personal use." But it is rather easy and tempting to bring substantial amounts of perfume and similar items back to the United States under a "personal use" pretense. While I cannot, of course, speak here in the name of our entire industry, I am inclined to believe that there would not be serious opposition to some relaxation of the present rule in cases of bona fide importation for personal use. Of course, abuses of this privilege could not be condoned. As you undoubtedly know, Senator Javits early this year introduced a bill intended solely for the benefit of the returning tourist (S. 542, 86th Cong., 1st Sess., introduced January 20, 1959, referred to the Committee on Finance). •

(*Continued from page 311*)

roughness. Antibacterial compounds, like hexachlorophene, bithionol and related derivatives, may reduce the incidence of minor skin infections that could contribute to skin roughness.

The second consumer requirement in importance is said to be absence of stickiness. This should not be especially difficult to meet, since it involves a negative approach—not too much of ingredients that might cause the trouble. As a supplementary note, oiliness or greasiness may be prevented in the same way, by the absence of too much.

The requirement for quick drying is also easily met by keeping low the proportions of slowly evaporating components, primarily humectants. Alcohol is sometimes added to hand lotions to accelerate evaporation and impart a cooling sensation to the hands. Alcohol, as a solvent, may also upset emulsion balance and the formula must be specifically devised on the basis of either the absence or presence of alcohol.

Of paramount importance is the composition and structure of the final deposit left on the skin after water has evaporated from the lotion or cream. It is not proper to assume that this deposit merely consists of all of the non-volatile components and none of the volatile ones; evaporation to an anhydrous level is unlikely and the proportion of water remaining will have a definite effect upon the properties of the film. I have seen no published report of the changes that take place in a cream or lotion as the water evaporates under circumstances comparable to those when the preparation is rubbed out on the skin. Nor have I seen any statement concerning the amount of water that can be expected to remain in the final deposit. This information might lead to superior products.

At any rate, the cream or lotion, especially if it contains substantial amounts of stearic acid, must contain a plasticizer. This prevents the film from becoming dry and brittle enough to roll on the skin instead of forming a uniform layer. Customary plasticizers also have a humectant function, retarding evaporation of a cream in an opened jar and to some extent keeping moisture in the film for absorption by the skin. These are usually glycerin, propylene glycol, and sorbitol, but it seems likely that some of the less hygroscopic polyethylene glycols could be added for effective plasticizing action.

Naturally, the perfume used must be a generally attractive one, must be non-irritating, and should not affect the stability of the emulsion nor be adversely affected by emulsion components—it should not cause discoloration nor undergo chemical odor changes. Another point to be considered is initial and final concentration. In a hand lotion especially, there may be about a tenfold concentration from the original lotion to the final film. A normal 0.5 per cent perfume concentration in the lotion may end as a too concentrated 5 per cent on the skin. Some of the perfume, of course, evaporates with the other volatile components, but the perfume may require special formulation to give the desired odor in the bottle and comparable quality and strength on the skin.

The color of the emulsion, although not covered in the questionnaire, is a factor in the over-all elegance of the product and its attractiveness to the consumer. A yellow or pink tint may cover an unattractive greyness or be attractive in itself by conveying the illusion of richness. A pure white emulsion, on the other hand, may convey the impression of skin whitening. The choice here may well be determined by market research or even the sales manager's hunch. Once color has been decided upon, however, it might as well be right. The dye (from the certified list) must be one that is stable in the preparation and be affected to a minimum extent by light. Tinting of internal and external phases by means of mixtures of oil- and water-soluble colors is sometimes advocated; this seems to be an unnecessary complication, possibly causing more trouble than advantage.

An attribute invisible to the consumer, but nevertheless of vital importance, is preservation. Attack by microorganisms may cause changes in color and odor and even cause complete breakdown of the lotion or cream. Attack by oxygen and development of rancidity must also be avoided. Sometimes preservation and prevention of rancidity is difficult, and the easiest way to handle the problem will be elimination of the offending ingredients. The preservative (and the antioxidant) should be colorless, odorless, non-irritating and should neither affect the preparation adversely nor be affected by it. Remember, too, that the usefulness of these agents is strongly affected by the *p*H of the vehicle: both preservatives and antioxidants are generally less effective in the alkaline range. The parahydroxy benzoic esters, alone or in mixtures, deserve their enduring popularity, since they have been repeatedly proved effective and harmless. A possible limitation of their use is that they seem to form complexes with some polyhydroxy compounds and thus lose preservative power. Sorbic acid seems to have some usefulness as an anti-mold compound. Antioxidants, to be dissolved in the oil to be protected, include NDGA, butylated hydroxyanisole and hydroxytoluene, and esters of gallic acid. The last, especially, may cause discoloration in alkaline aqueous media.

Finally, the problems of the chemist and the ingenious ways in which he solves them are of no concern to the consumer, nor to the management employing the chemist. What is important is that a product be developed that will do desirable things to the skin or hair surface to which it is applied, or at least give the illusion of doing these desirable things. Emulsion stability and attractive consistency must be taken for granted as the least an effective chemist can do. The emulsion must be the vehicle permitting the application of the film that will provide what the consumer seeks. •

COMING EVENTS . . . . .

SEPTEMBER

13-18 **American Chemical Society,** national meeting, Atlantic City, N. J. (Alden H. Emery, Executive Secretary, 115 Sixteenth St., N.W., Washington 6, D.C.)

14-17 **Associated Chain Drug Stores,** Associated-Benedikt fall meeting, Park Sheraton Hotel, New York City (Harry J. Towers, A.C.D.S., 245 Fifth Ave., N. Y. C. 16)

16 **Society of Pharmacists in Industry,** fall meeting, New York Academy of Sciences, 2 East 63rd Street, N. Y. C. (Vincent de Feo, Dodge & Olcott, Inc., 180 Varick St., N. Y. C. 14)

17-20 **Drug, Chemical & Allied Trades Section, New York Board of Trade,** annual meeting, Sagamore Hotel, Bolton Landing, Lake George, N. Y. (Helen I. Booth, D.C.A.T., 291 Broadway, N. Y. C 7)

20-23 **The Proprietary Assn. of Canada,** annual general meeting and convention, The Chantecler, Ste. Adele-en-haut, P.Q. (Mrs. Agnes Howard, P.A.C., 252 Eglinton Ave. East, Toronto 12, Ontario)

20-24 **National Assn. of Retail Druggists,** annual national convention, St. Louis, Mo. (N.A.R.D., 205 W. Wacker Drive, Chicago 6, Ill.)

23-24 **Society of Cosmetic Chemists,** annual cosmetic seminar, French Institute and New York Academy of Sciences, New York City (Walter Wynn, S.C.C., The New York Academy of Sciences, 2 E. 63rd St., N.Y.C. 21)

24-25 **American Society for Quality Control,** Chemical Division annual conference, Shamrock Hilton Hotel, Houston, Texas.

28 **Salesmen's Assn. of the American Chemical Industry,** annual sales clinic, Roosevelt Hotel, N.Y.C. (S.A.A.C.I., 60 E. 42nd St, N.Y.C. 17)

28 **Instrument Symposium and Research Equipment Exhibit** (through Oct. 1) National Institutes of Health, Bethesda, Md. (James B. Davis, N.I.H., Bethesda, Md.)

28-30 **American Management Assn.,** seminar on packaging line layout, Hotel Astor, N.Y.C. (A.M.A., 1515 Broadway, N.Y.C. 36)

28-30 **American Oil Chemists' Society,** Hotel Statler, Los Angeles, Calif

OCTOBER

1-2 **Society of the Plastics Industry,** New England Section conference, Wentworth-by-the-Sea, Portsmouth, N. H. (S.P.I., 250 Park Ave., N.Y.C. 17)

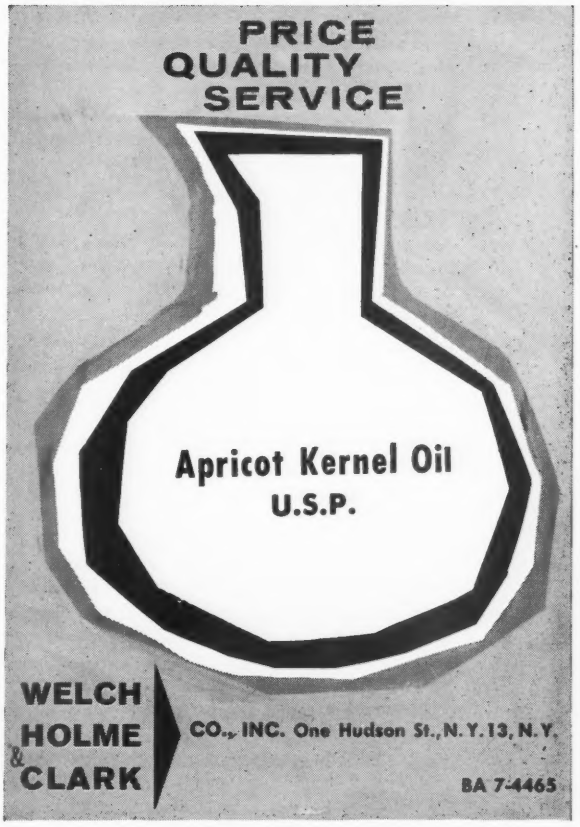
11-16 **Pan-American Pharmaceutical and Biochemical Federation,** seminar on pharmaceutical education, San Juan Intercontinental Hotel, San Juan, Puerto Rico (Dr. Melvin W. Green, American Council on Pharmaceutical Education, 77 Washington St., Chicago 2, Ill.

14-16 **Pharmaceutical Manufacturers Assn.,** Biological Section, Drake Hotel, Chicago, Ill. (Dr. Karl Bambach, P.M.A., 1411 K Street, N.W., Washington 5, D.C.)

14-16 **Parenteral Drug Assn.,** annual convention, Statler Hotel, N. Y. C. (Hubert E. Boyden, P.D.A., 4865 Stenton Ave., Philadelphia 44, Penna.)

16 **National Vitamin Foundation,** symposium on the role of vitamins and other nutrients in lipid metabolism, Auditorium, Tulane University School of Medicine, New Orleans, La. (N.V.F., 149 E. 78th St., N. Y. C. 21)

(Continued on page 418)



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17-25 **International Fair of the Plastics Industry** (for producers, processors, machinery manufacturers), Dusseldorf, Germany (German-American Chamber of Commerce, Inc., 350 Fifth Ave., N. Y. C. 1)

19-23 **National Safety Council,** national congress ad exposition, Chicago, Ill. (R. L. Forney, N.S.C., 425 N. Michigan Ave., Chicago 11, Ill.)

19-23 **American Public Health Assn.,** annual meeting, Convention Hall, Atlantic City, N. J.

20-21 **Pharmaceutical Manufacturers Assn.,** Pharmaceutical Contact Section, Washington Hotel, Washington, D.C. (Dr. Karl Bambach, P.M.A., 1411 K Street, N.W., Washington 5, D.C.)

22-23 **Pharmaceutical Manufacturers Assn.,** Production and Engineering Section, Van Cleve Hotel, Dayton, Ohio (See above.)

25-28 **National Flexible Packaging Assn.,** fall meeting, White Sulphur Springs, West Virginia)

25-28 **Pharmaceutical Manufacturers Assn.,** Financial Section, Greenbrier Hotel, White Sulphur Springs, W. Va. (See above.)

NOVEMBER

1-5 **German Society of Cosmetic Chemists,** scientific and cosmetic sessions, Baden-Baden, Germany (Dr. Herbert Neugebauer, Baden-Baden, Metzgerstrasse 30, Germany)

2-4 **American Management Assn.,** seminar on manufacturing's part in the packaging program, Hotel Astor, N.Y.C. (A.M.A., 1515 Broadway, N.Y.C. 36)

2-4 **American Management Assn.,** seminar on printing on packaging, Hotel Astor, N.Y.C. (See above.)

2-4 **Pharmaceutical Manufacturers Assn.,** Research and Development Section, Greenbrier Hotel, White Sulphur Springs, W. Va. (Dr. Karl Bambach, P.M.A., 1411 K Street, N.W., Washington 5, D.C.)

3 **1959 Exposition of Chemical Industry,** Coliseum, N. Y. C. (through December 4)

3-5 **Packaging Assn. of Canada,** national packaging exposition, Automotive Building, Exhibition Grounds, Toronto, Canada

4-6 **Symposium on Antibiotics,** Mayflower Hotel, Washington, D. C. (Dr. Henry Welch, Director, Div. of Antibiotics, F. D. A., U. S. Dept. Health, Education, and Welfare, Washington 25, D. C.)

7-12 **National Wholesale Druggists' Assn.,** annual convention, Americana Hotel, Bal Harbour, Fla. (Harry A. Kimbriel, N.W.D.A., 60 East 42nd St., N. Y. C. 17)

9-11 **American Management Assn.,** seminar on fundamentals of packaging specifications, Hotel Astor, N.Y.C. (See above.)

9-12 **Glass Container Manufacturers Institute,** fall meeting, Arizona-Biltmore Hotel, Phoenix, Arizona (H. W. Kuni, 99 Park Ave., N. Y. C. 6)

12-14 **Gerontological Society,** Statler Hotel, Detroit (Administrative Secretary, Mrs. Marjorie Adler, 660 S. Kingshighway Blvd., St. Louis 10, Mo.)

16-18 **Packaging Institute,** annual national packaging forum, Hotel Statler, N. Y. C. (Charles A. Feld, P.I., 342 Madison Ave., N. Y. C. 17)

16-20 **Fifth International Automation Congress and Exposition,** New York Trade Show Bldg., New York City.

17-20 **Packaging Machinery Manufacturers Institute Show,** New York Coliseum, N. Y. C. (Albert R. Stevens, Elgin Mfg. Co., Inc., Elgin, Ill.)

24 **Manufacturing Chemists' Assn.,** Statler Hilton Hotel, New York City (M. F. Crass, M.C.A., 1825 Connecticut Ave., N.W., Washington 9, D. C.)

30 **Exposition of the Chemical Industries, New York** Coliseum (E. K. Stevens, International Exposition Co., 480 Lexington Ave., N.Y.C. 17)

DECEMBER

1 **Toilet Goods Assn.,** scientific section, winter meeting, Waldorf-Astoria Hotel, N. Y. C. (Kathryn Fitzpatrick, Americas Bldg., Rockefeller Center, N. Y. C. 20)

2 **Synthetic Organic Chemical Manufacturers Assn.,** annual meeting and dinner, Hotel Roosevelt, New York City (S. Stewart Graff, Sec., S.O.C.M.A., 41 East 42nd St., N. Y. C. 17).

7-9 **Pharmaceutical Manufacturers Assn.,** mid-year and eastern regional meeting, Waldorf-Astoria Hotel, N. Y. C. (J. O'Neill Closs, P.M.A., 1411 K Street, N.W., Washington 5, D.C.)

7-9 **Chemical Specialties Manufacturers Assn.,** annual meeting and aerosol package contest, Mayflower Hotel, Washington, D.C. (C.S.M.A., 50 E. 41st St., N.Y.C. 17)

7-10 **American Medical Assn.,** clinical meeting, Dallas Auditorium, Dallas, Texas

9 **The Proprietary Assn.,** Research and Scientific Development meeting, Hotel Roosevelt, New York City (Dr. Howard A. Prentice, 810 18th St., N.W., Washington 6, D.C.)

1960

JANUARY

9 **Northwest Society for Clinical Research,** Seattle, Washington (Dr. John R. Hogness, 721 Minor Ave., Seattle 4, Wash.)

11-13 **American Academy of Allergy,** Hollywood Beach Hotel, Hollywood Fla. (James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wisc.)

FEBRUARY

3-5 **Pharmaceutical Manufacturers Assn.,** Legislative Section, Boca Raton, Fla. (Dr. Karl Bambach, P.M.A., 1411 K Street, N.W., Washington 5, D.C.)

8-10 **Pharmaceutical Manufacturers Assn.,** central regional meeting, Edgewater Beach Hotel, Chicago, Ill. (J. O'Neill Closs, 1411 K Street, N.W., Washington 5, D.C.)

15-16 **Pharmaceutical Manufacturers Assn.,** western regional meeting, Ambassador Hotel, Los Angeles, Calif. (J. O'Neill Closs—see above.)

25-27 **Symposium on Fundamental Cancer Research,** Univ. of Texas, Houston, Texas (Univ. of Texas, M.D. Anderson Hospital and Tumor Institute, Houston 5, Texas)

28 **American College of Allergists** (through March 5) Americana Hotel, Bal Harbour, Miami Beach, Fla. (Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Minn.)

MARCH

2-4 **Pharmaceutical Manufacturers Assn.,** Medical Section, Hollywood Beach Hotel, Hollywood Fla. (Dr. Karl Bambach—see above.)

3 **Drug, Chemical and Allied Trades Section, New York Board of Trade, Inc.,** annual dinner (Helen L. Booth, D.C.A.T., 291 Broadway, N. Y. C. 7)

13-18 **National Health Council,** national health forum, Miami, Fla. (Philip E. Ryan, 1790 Broadway, N.Y.C. 19)

15-16 **American Broncho-Esaphogological Assn.,** Deauville Hotel, Miami Beach, Fla. (Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Penna.)

15-17 **American Laryngological, Rhinological and Otological Society,** Deauville Hotel, Miami Beach, Fla. (Dr. C. Stewart Nash, 708 Medical Arts Building, Rochester 7, N.Y.)

(Continued on page 419)

18-19 **American Laryngological Assn.**, Deauville Hotel, Miami Beach, Fla. (Dr. Lyman Richards, Massachusetts Institute of Technology, Cambridge 39, Mass.)

APRIL

1-2 **American Gastroenteral Assn.**, Roosevelt Hotel, New Orleans, La. (Dr. Wade Volwiler, Dept. of Medicine, University of Washington, Seattle, Wash.)

1-3 **American Society of Internal Medicine**, Mark Hopkins Hotel, San Francisco, Calif. (Robert L. Richards, 350 Post St., San Francisco 8, Calif.)

2-6 **American College of Obstetricians and Gynecologists**, Netherland Hilton Hotel, Cincinnati, Ohio (Donald F. Richardson, P. O. Box 749, Chicago 90, Ill.)

4-7 **American Management Assn.**, national packaging exposition, Convention Hall, Atlantic City, N.J. (Packaging Exposition, Clapp & Poliak, Inc., 341 Madison Ave., N.Y.C. 17)

5-14 **American Chemical Society**, spring national meeting, Cleveland, Ohio (A. T. Winstead, A.C.S., National Meetings Dept., 1155 Sixteenth St., N.W., Washington 6, D. C.)

8-12 **American Dermatological Assn.**, Boca Raton Hotel, Boca Raton, Fla. (Dr. Wiley M. Sams, 308 Ingraham Bldg., Miami 32, Fla.)

11-15 **American Assn. of Immunologists**, Chicago, Ill. (Dr. Calderon Howe, Columbia University College of Physicians and Surgeons, N.Y.C. 22)

11-16 **American Society of Biological Chemists**, Chicago, Ill. (Dr. Frank W. Putnam, Dept. of Biochemistry, Univ. of Fla., Gainesville, Fla.)

28-30 **American Assn. of Pathologists and Bacteriologists**, Hotel Peabody, Memphis, Tenn. (Dr. Russell L. Holman, Dept. of Pathology, L.S.U. School of Medicine, New Orleans, La.)

MAY

11 **Toilet Goods Assn.**, Scientific Section, Waldorf-Astoria Hotel, N.Y.C. (Kathryn Fitzpatrick, Americas Bldg., Rockefeller Center, N.Y.C. 20)

8-11 **Proprietary Association**, annual meeting, The Greenbrier, White Sulphur Springs, W. Va. (Dr. Howard A. Prentice, 810 18th St., N.W., Washington 6, D.C.

16-18 **Chemical Specialties Manufacturers Assn.**, mid-year meeting, Drake Hotel, Chicago, Ill. (C.S.M.A., 50 E. 41st St., N.Y.C 17)

JUNE

12-15 **Extension Services in Pharmacy**, annual national industrial pharmaceutical research conference (stabilization and stability testing of pharmaceuticals), King's Gateway. Land O' Lakes, Wisc. (Richard S. Strommen, E.S.P., Univ. of Wisconsin, Madison, Wisc.)

27-30 **Toilet Goods Assn.**, annual convention, Poland Spring, Maine, (Kathryn Fitzpatrick, Americas Bldg., Rockefeller Center, N.Y.C. 20)

JULY

19-21 **Western Packaging & Materials Handling Exposition**, Pan Pacific Auditorium, Los Angeles, Calif. (Western Packaging Exposition, Clapp & Poliak, Inc., 341 Madison Ave., N. Y. C. 17)

SEPTEMBER

11-16 **Americal Chemical Society**, fall national meeting, New York City (A. T. Winstead, A.C.S., National Meeting Dept., 1155 Sixteenth St., N.W., Washington 6, D.C.) •

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